# THE American JOURNAL OF Surgery

JUNE 1955

THURSTON SCOTT WELTON, M.D., EDITOR

## A Commemorative Issue

*Dedicated to*

## Emile F. Holman, M.D.

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Index Issue Vol. 89

SIXTY-FOURTH YEAR OF PUBLICATION

JUNE 1955

# THE American JOURNAL OF Surgery

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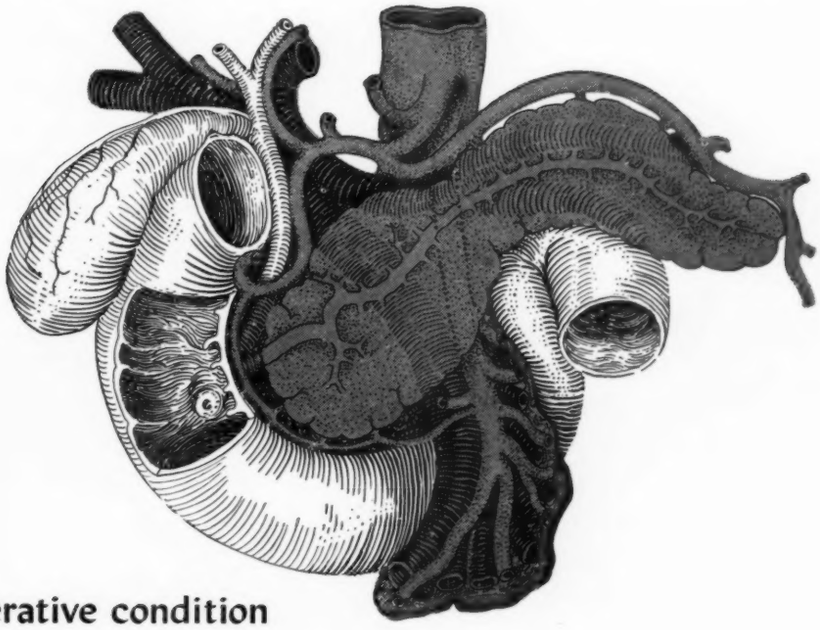
## in biliary surgery



## improves preoperative condition

- flushes liver stones into surgical zone[2]
- protects against liver injury[3]

## enhances postoperative results

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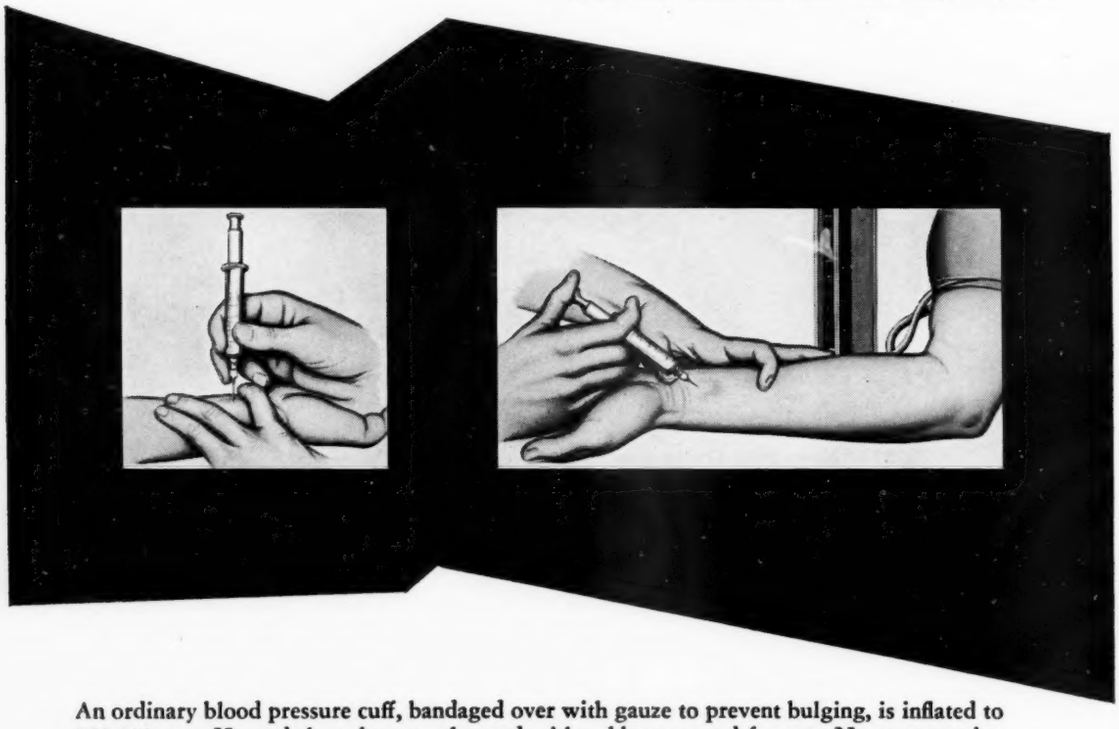

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# The American Journal of Surgery

## *CONTENTS–June 1955*

VOLUME EIGHTY-NINE NUMBER SIX

Emile F. Holman, M.D. . . . . 1089
*LOREN R. CHANDLER*

A Tribute. . . . . 1093
*ANN PURDY*

The Brigham in Emile Holman's Day . . . . 1094
*FRANCIS D. MOORE*

*EDITORIAL*

A Patient or a Case . . . . . 1099
*GEORGE D. BROWN*

*SCIENTIFIC PAPERS*

The Physiology of an Arteriovenous Fistula . . . 1101
*EMILE HOLMAN*

Some Problems of Peptic Ulcer . . . . . 1109
*ARTHUR L. BLOOMFIELD*

Evaluation of Results of Digital Flexor Tendon Grafts . . . . . 1116
*JOSEPH H. BOYES*

*Contents Continued on Page 5*

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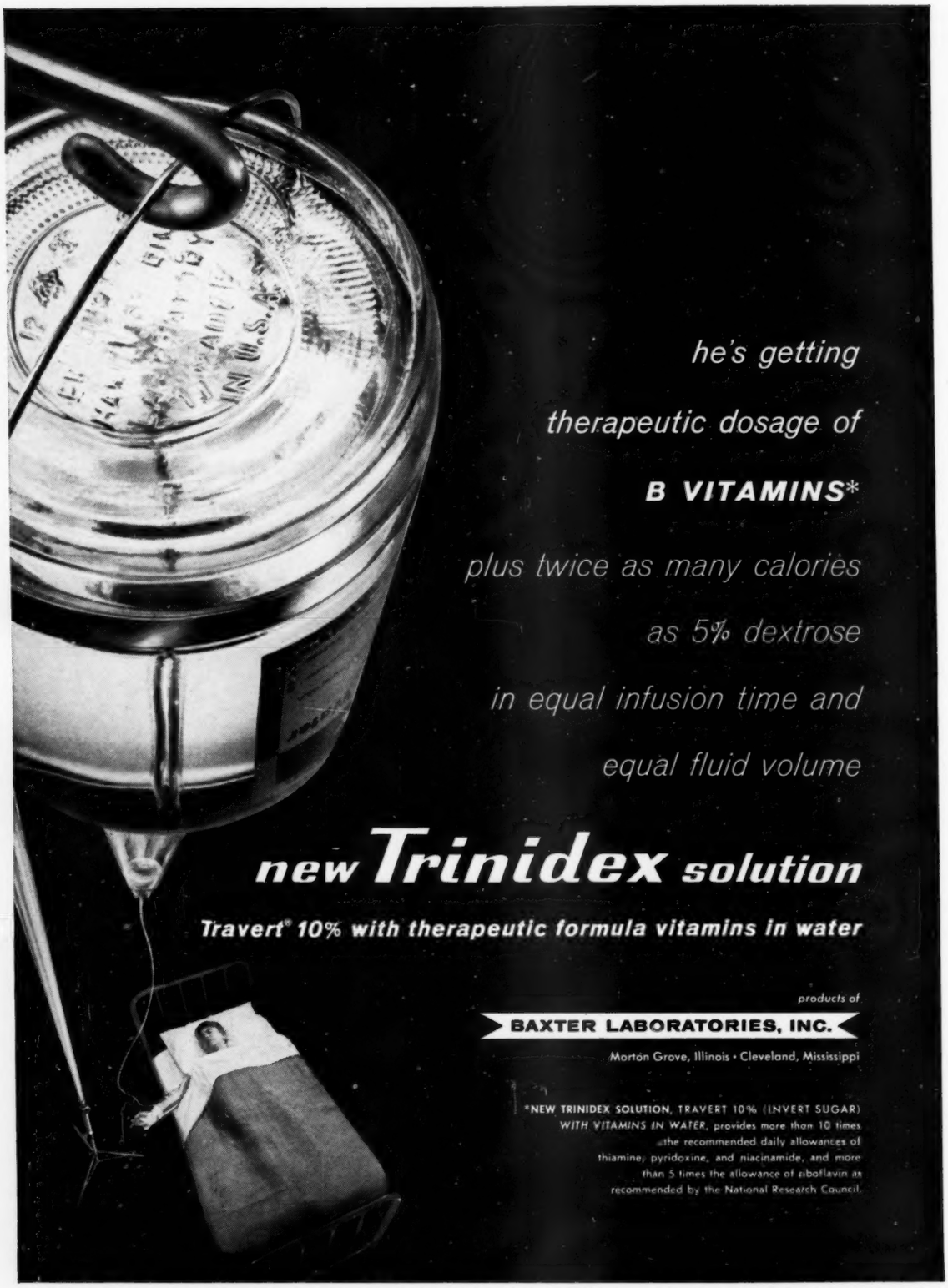
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# *CONTENTS continued–June 1955*

VOLUME EIGHTY-NINE NUMBER SIX

Massive Gastrointestinal Hemorrhage in the Presence of Portacaval Anastomosis . . . . . 1120
*ROY COHN*

Hypertrophic Pyloric Stenosis in the Adult . . . 1123
*JOHN E. CONNOLLY*

Prepubertal Malignant Melanomas. Report of Two Cases . . . . . 1128
*LEONARD DOBSON*

Gastric Resection. A Compilation of Technics . . 1136
*EDWARD W. DOHERTY*

Surgical Treatment of Coarctation of the Aorta in Infancy. Report of Two Cases . . . . . 1138
*FRANK GERBODE, ANN PURDY, ROBERT H. ALWAY, JOHN J. PIEL AND ISEU AFFONSO DA COSTA*

Unilateral Exophthalmos Due to Orbitofrontal Cholesterol Granuloma . . . . . 1144
*JOHN W. HANBERY AND MARK RAYPORT*

Surgical Treatment of Rheumatic Tenosynovitis . 1163
*LOT D. HOWARD, JR.*

Embolic Grafts in the Lungs of Dogs . . . . 1169
*PHILLIPS JOHNSON*

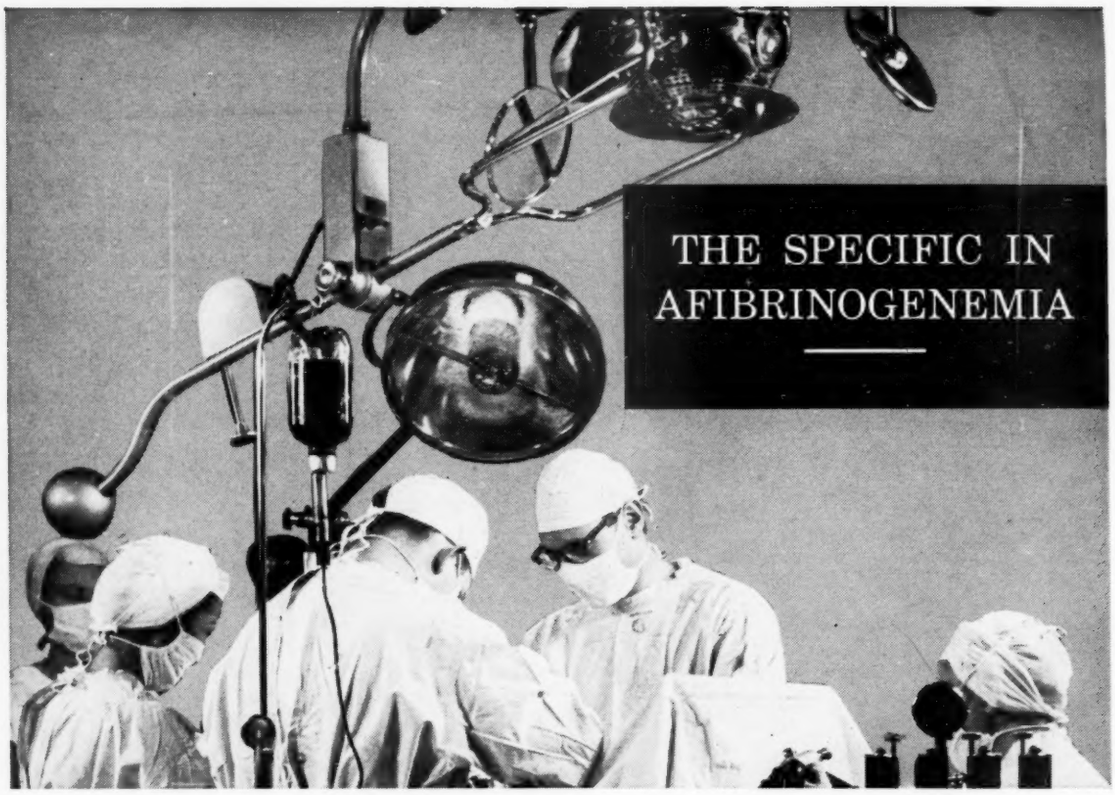
Iliac Thrombophlebitis—Visualization Prior to Ligation. Case Report . . . . . 1172
*JAMES W. MARTIN*

Surgical Significance of Gastrointestinal Bleeding . 1177
*CARLETON MATHEWSON, JR. AND BENJAMIN SUGAR*

Subtotal Gastric Resection for Peptic Ulcer. Historical Review with the Description of a Variation in Technic . . . . . 1182
*GUNTHER W. NAGEL*

Rhabdomyoma of Skeletal Muscle. Report of a Case 1187
*HARRY G. PARSONS AND HENRY E. PURO*

*Contents Continued on Page 7*

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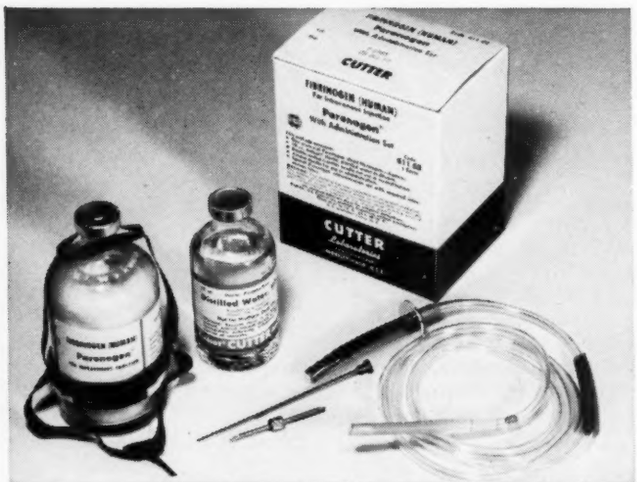


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# *CONTENTS continued–June 1955*

VOLUME EIGHTY-NINE NUMBER SIX

End Result of Using Vitallium Tubes in Common Duct Strictures . . . . . 1191
*HERMAN E. PEARSE*

Vascular Replacements and Reconstruction Utilizing Inert Material . . . . . 1196
*EDGAR J. POTH, JOHN H. CHILDERS, JOSEPH K. JOHNSON AND ROBERT S. GUY*

Atypical Neuralgias of the Head. Headaches, So-called Migraine and Complications of Whiplash Injuries and Other Cervical Trauma . . . . . 1203
*FREDERICK LEET REICHERT*

Surgery of the Adrenals. . . . . 1212
*VICTOR RICHARDS*

Surgical Treatment of Chronic Ulcerative Colitis. . 1224
*ROBERT A. SCARBOROUGH*

Treatment of Annular Pancreas . . . . . 1230
*FREDERIC P. SHIDLER*

Surgical Treatment of Coarctation of the Aorta. Further Experiences with the Use of the Subclavian Artery. . . . . 1235
*HARRIS B. SHUMACKER, JR.*

Aneurysm of the Hepatic Artery. Report of Three Cases . . . . . 1241
*JOHN H. STEELQUIST*

Author Index to Volume 89 . . . . . 1245

Subject Index to Volume 89 . . . . . 1247

*NOTES AND QUOTES (Advertising Section)* . . 38

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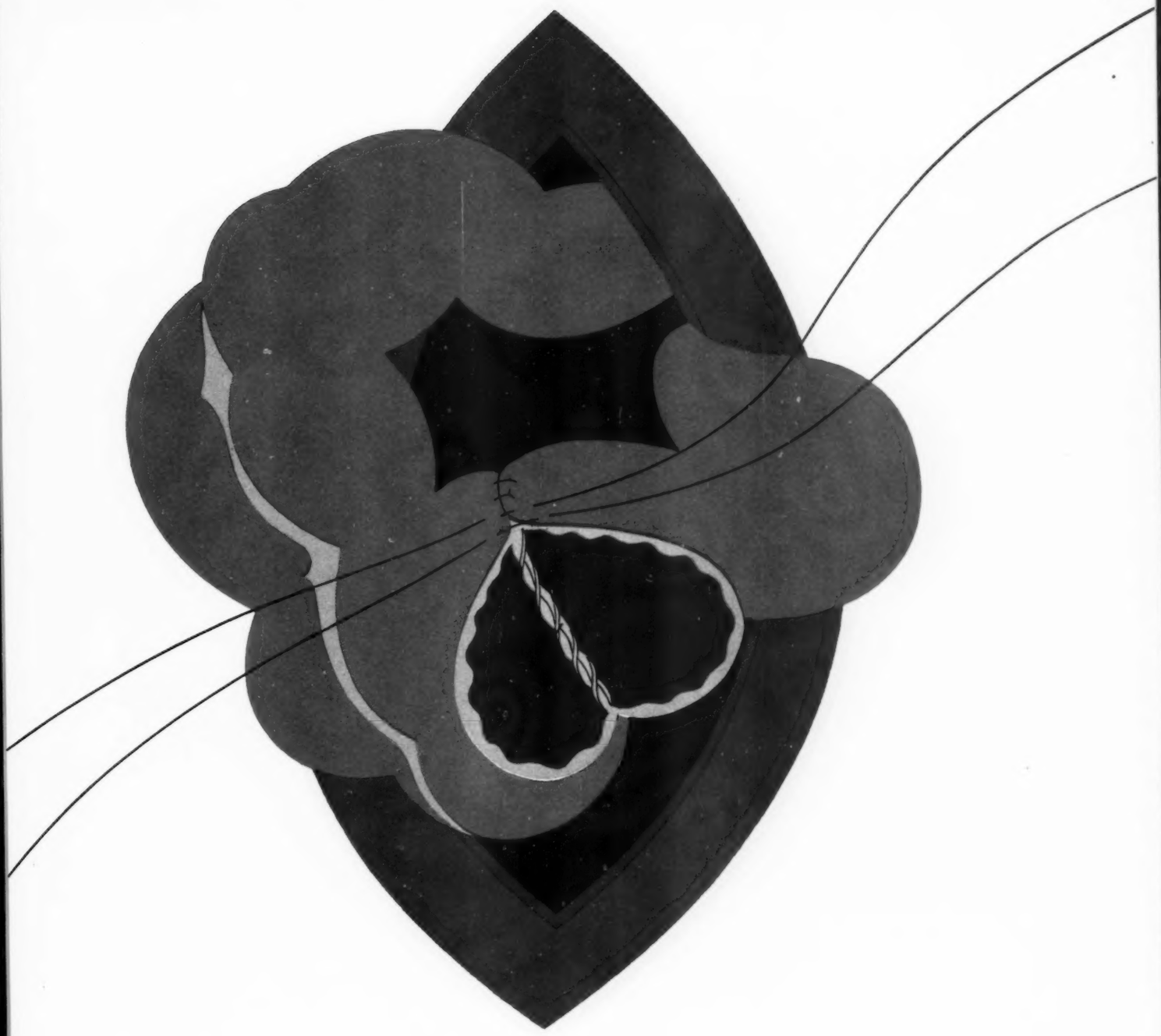

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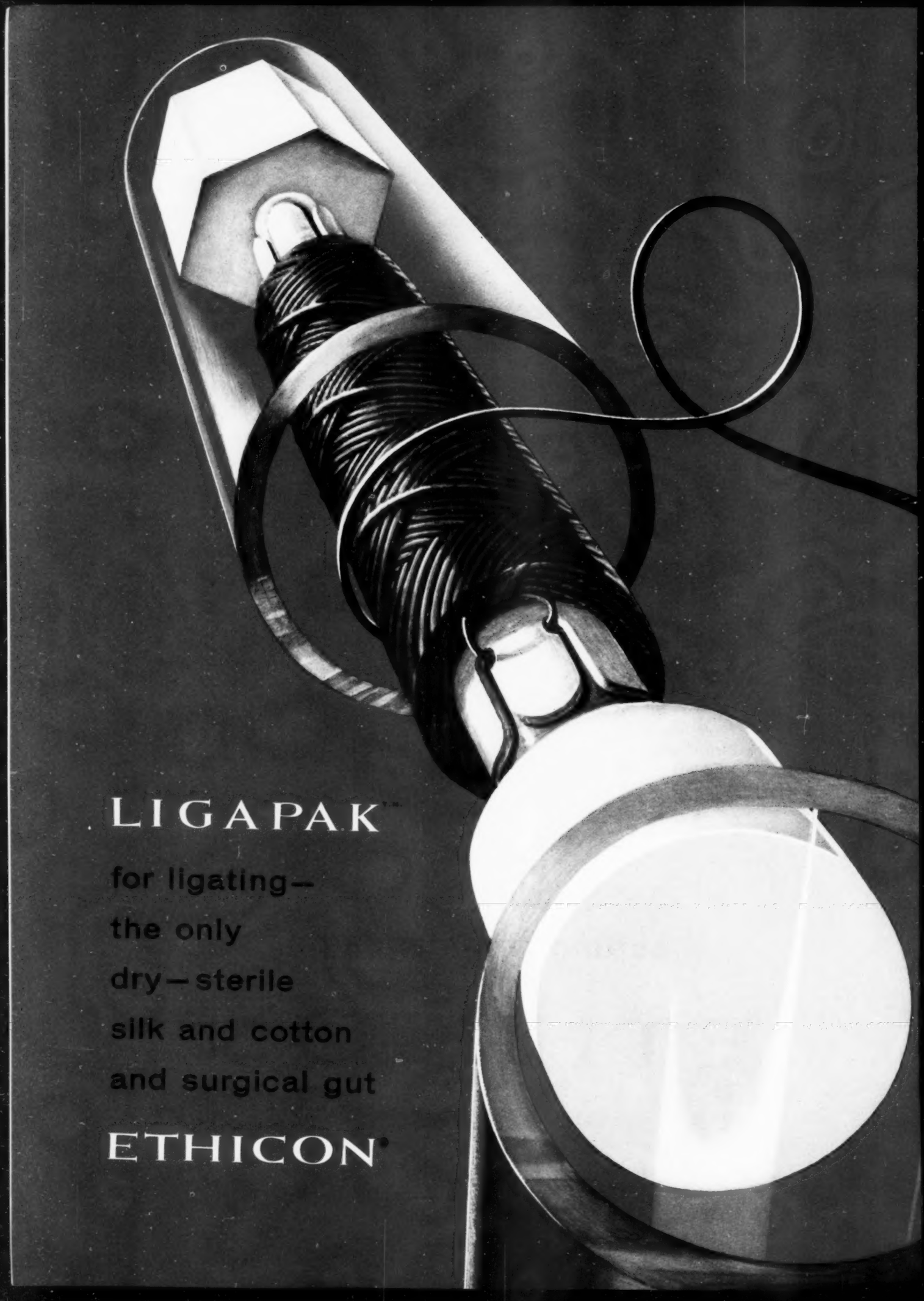
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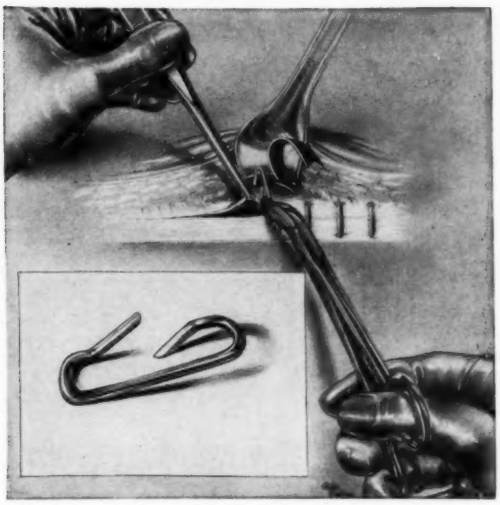

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*Cincinnati General Hospital*

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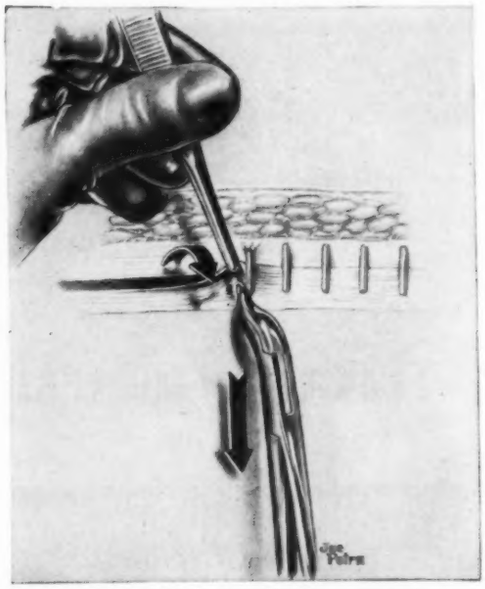

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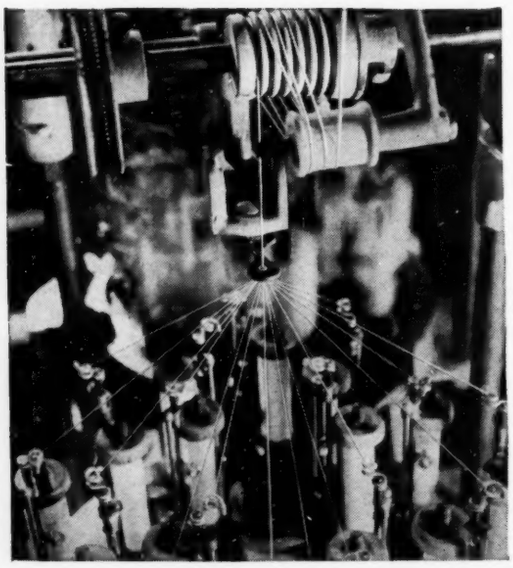

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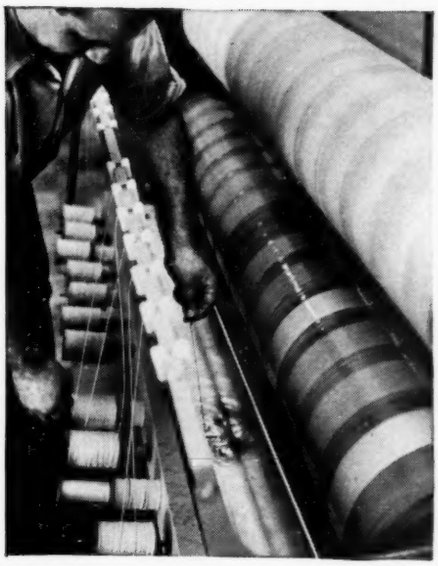

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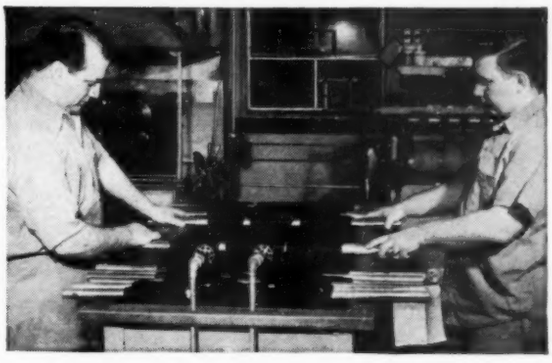

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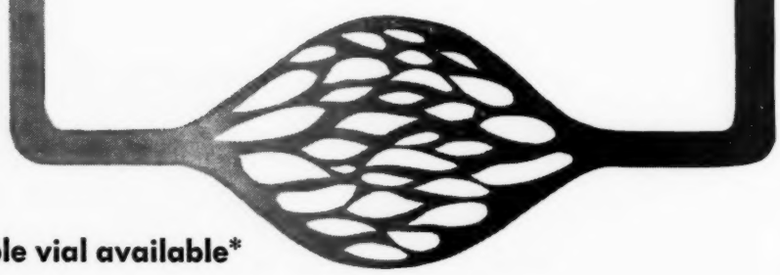

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# When you specify the Pfizer antibiotic of your choice *Stress Fortified* with the B-complex, C and K vitamins recommended by the National Research Council, be sure to write SF* on your prescription

antibiotics *Stress Fortified* with vitamins include:

## ®Terramycin-SF

*Brand of oxytetracycline with vitamins*

CAPSULES 250 mg.

## ®Tetracyn-SF

*Brand of tetracycline with vitamins*

CAPSULES 250 mg.

ORAL SUSPENSION (fruit flavored)
125 mg./5 cc. teaspoonful

**The minimum daily dose of each antibiotic** *(1 Gm. of Terramycin or Tetracyn, or 600,000 units of penicillin)*
**Stress Fortifies the patient** *with the stress vitamin formula* **recommended by the National Research Council:**

| | | | |
|---|---|---|---|
| Ascorbic acid, U.S.P. | 300 mg. | Calcium pantothenate | 20 mg. |
| Thiamine mononitrate | 10 mg. | Vitamin $B_{12}$ activity | 4 mcg. |
| Riboflavin | 10 mg. | Folic acid | 1.5 mg. |
| Niacinamide | 100 mg. | Menadione (vitamin K analog) | 2 mg. |
| Pyridoxine hydrochloride | 2 mg. | | |

**Trademark*

Pfizer

PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N. Y.

# Adrenosem®

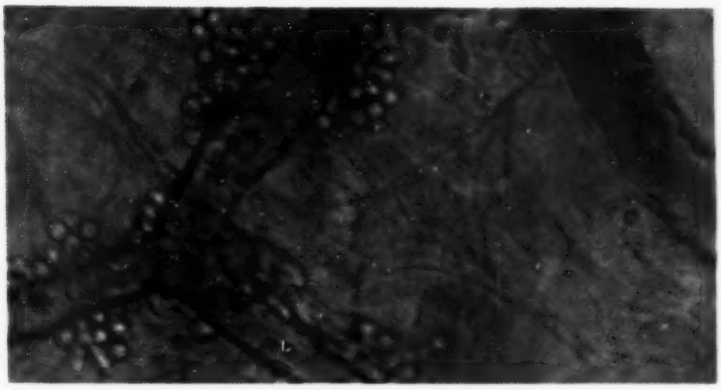
SALICYLATE

*(Brand of carbazochrome salicylate)*

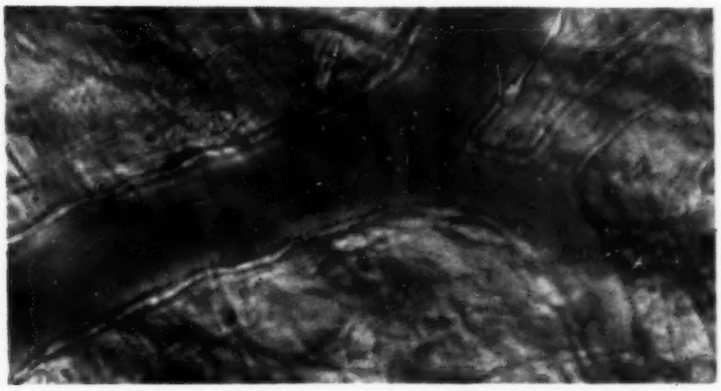
The unique systemic hemostat

**Adrenosem checks bleeding by decreasing capillary permeability and promoting retraction of severed capillary ends. It aids in maintaining capillary integrity by direct action on the capillary walls.**

**Adrenosem does not alter blood components, nor does it affect blood pressure or cardiac rate. No toxic reactions have been reported in more than two years of clinical use.**



*Trauma from snake venom produces hemoconcentration and stasis, indicative of altered vascular permeability.*



*Trauma does not produce petechiae following Adrenosem injection.*

## VISUAL PROOF OF ADRENOSEM'S EFFECTIVENESS

To confirm the action of Adrenosem, the cheek pouch of a hamster was irritated with snake venom, which has the property of making the capillaries more permeable. A great many petechiae appeared on the surface and a 500X magnification showed the capillaries with extravasation of erythrocytes. Another animal was treated with Adrenosem, and 30 minutes later, the same amount of snake venom was used to irritate the cheek pouch. Microphotographs show the capillary walls intact and the blood cells coursing through the capillaries, without signs of escaping erythrocytes.

## SUPPLY

Ampuls, 5 mg., 1 cc.: packages of 5.
Tablets, 1 mg. (s.c. orange): bottles of 50.
Tablets, 2.5 mg. (s.c. yellow): bottles of 50.
Syrup, 2.5 mg. to each 5 cc. (1 teaspoonful): 4 oz. bottles

## REFERENCES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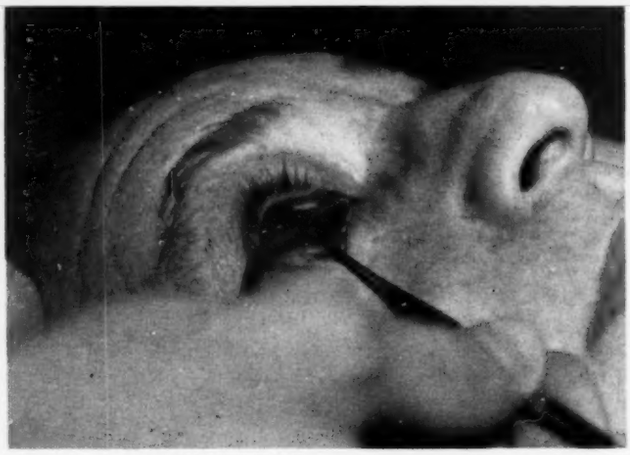
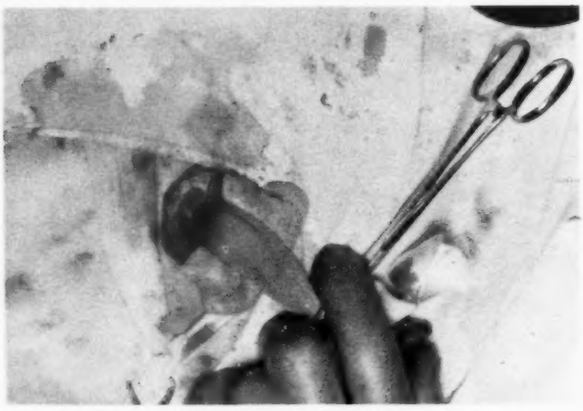


*Welling up of blood upon incision of lid and conjunctiva, coming in ophthalmic procedures, hampers surgery.*

*Minimal bleeding after Adrenosem therapy facilitates surgery and promotes healing.*

*Mastoidectomy with a bloody field obscures view, requires frequent suctioning.*



*After Adrenosem therapy. Note clearer operative field with minimized bleeding.*

Detailed literature on request

# Adrenosem®

**SALICYLATE**

*(Brand of carbazochrome salicylate)*

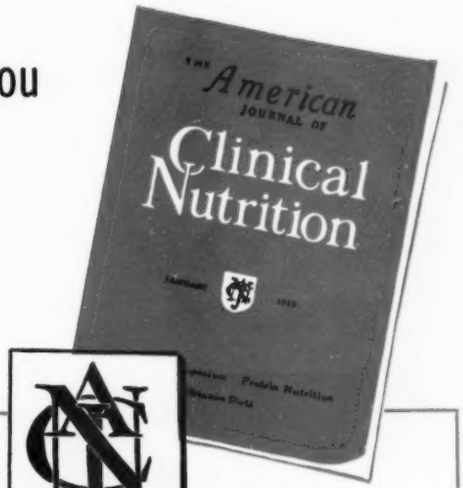
## DOSAGE

- preoperatively to control oozing during surgery and provide clearer operative field: one to two ampuls (5 to 10 mg.) every two hours prior to surgery for two doses.
- postoperatively to prevent hemorrhage and check oozing:
one to two ampuls (5 to 10 mg.) every two hours until there is no indication of undue bleeding. To maintain control, one ampul may be administered every three hours or 1 to 5 mg. orally t.i.d.
- to control active bleeding:
one ampul (5 mg.) every two hours until bleeding is controlled; frequency of dose may then be diminished.
- to control mild, low-grade bleeding:
one ampul (5 mg.) every three or four hours until bleeding is controlled; then 1 to 5 mg. orally four to five times daily until bleeding ceases.
- maintenance dosage to prevent bleeding in conditions where small vessel integrity may be impaired:
1 to 5 mg. orally t.i.d.; if bleeding ensues, dosage may be increased 1 to 5 mg. orally every three or four hours; if bleeding persists, oral dosage should be supplemented with one ampul (5 mg.) daily.
- pediatric dosage:
up to four years of age—1 mg. intramuscularly or orally with same frequency as for adults, until bleeding is controlled. From four to twelve years of age—one-half the adult dosage as indicated.

**THE S. E. MASSENGILL COMPANY**

BRISTOL, TENNESSEE • NEW YORK • KANSAS CITY • SAN FRANCISCO

Published exclusively to help you meet the **DIETARY PROBLEMS** of your patients because—




the TOTAL CARE of every patient includes **NUTRITION**

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new intravenous
technique for radiographic
delineation of the
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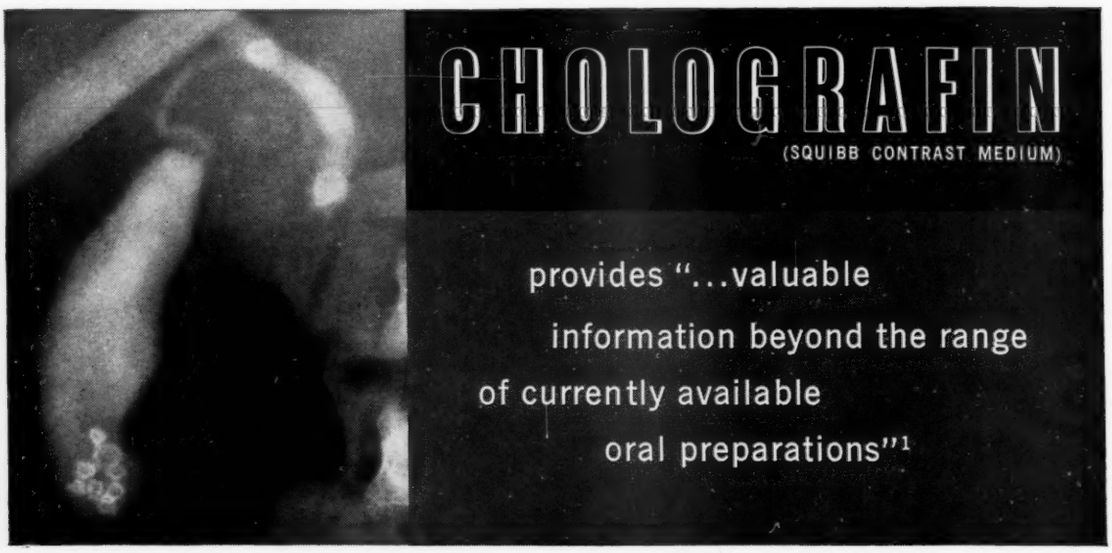
biliary system




- For demonstration of common duct stones and residual duct stumps *in the postcholecystectomy syndrome.*
- *As a preoperative measure* for visualization of suspected or unsuspected calculi in the common duct.
- As a complementary technique when oral contrast media fail to depict a gallbladder or common duct.
- Roentgenographic examination of the extrahepatic biliary system *in children.*
- Visualization of the common bile duct for evidence of displacement or obstruction *when a tumor is suspected near the porta hepatis.*
- For speedy radiographic study of the extrahepatic biliary system *when a rapid diagnosis is essential.*

*Cholografin is supplied in cartons of two 20-ml. ampuls, with two 1-ml. ampuls for sensitivity testing.*

1. Glenn, F., Evans, J., Hill, M., and McClenahan, J.: Ann. Surg. 140:600, 1954.

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*Ease of application*

*Transparency*

*Flexibility and*

*Minimal redressing*

distinguish

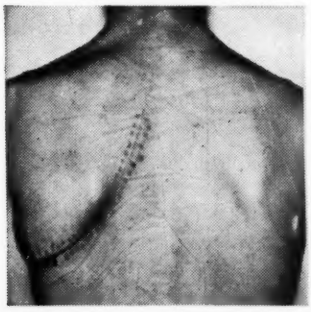
# AEROPLAST®

Brand of Vibesate

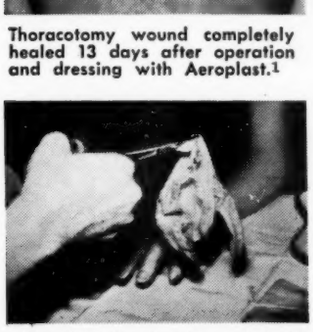
**LIQUID SURGICAL DRESSING**

Face laceration dressed with Aeroplast healed in four days.[2]

Bilateral inguinal hernia incisions protected by Aeroplast 4th post-operative day.[1]



Thoracotomy wound completely healed 13 days after operation and dressing with Aeroplast.[1]



Aeroplast dressing is peeled off like a glove 12 days after 2nd degree burn.[2]

*Sprayed directly onto the lesion from an aerosol "bomb," Aeroplast forms a protective plastic film dressing over any body contour. Aseptic lesions remain sterile as long as the dressings are intact. Aeroplast dressings are impermeable to bacteria. To remove, Aeroplast is simply peeled off.*

Rigler and Adams[1] dressed 110 operative wounds (including thoracotomies, laparotomies, inguinal hernias and miscellaneous lesions) with Aeroplast. "A single application sufficed in all but fifteen cases. No instances of systemic or clear-cut reactions were observed. Satisfactory results, with no evidence of erythema, infection, or necrosis were obtained in the majority of cases."

In 39 miscellaneous wounds dressed with Aeroplast (including appendectomies, open reduction of fractures, skin graft donor sites, lacerations, excoriation), Choy[2] reports infection in only one case, which promptly cleared with redressing, and uneventful healing in all others.


1. Rigler, S. P. and Adams, W. E.: Experience with a new sprayable plastic as a dressing for operative wounds, Surg. 36:792 (Oct.) 1954. (University of Chicago Clinics, Chicago, Surgical Service).

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*Supplied in 6 oz. aerosol-type dispenser through your prescription pharmacy or surgical dealer.*

*For reprints and literature write to:*

Aeroplast® CORPORATION

**416 DELLROSE AVENUE, DAYTON 3, OHIO**

Upjohn

# preoperative bowel preparation within 24 hours:

# Mycifradin *tablets*

Trademark for the Upjohn brand of neomycin

**Each tablet contains 0.5 Gm. neomycin sulfate (equivalent to 0.35 Gm. neomycin base). In bottles of 20 tablets.**

***Also available:***

**Mycifradin Sulfate Powder (topical) in vials of 0.5 Gm. and 5 Gm.**

**Mycifradin Sulfate (intramuscular) in vials of 0.5 Gm.**

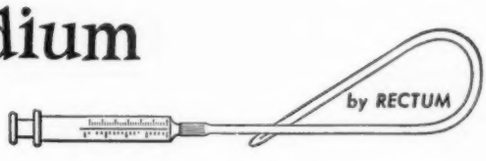
THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

# No Nightmare of Fear

**no pain, no memory...** for your pediatric patient never sees the operating room. With PENTOTHAL Sodium administered rectally, he goes to sleep in his own bed, wakes there afterward. In its many other uses—as an adjunct to general anesthesia, as sole agent in minor procedures—Rectal PENTOTHAL affords a simple, painless, always humane method of quieting frightened children. Abbott

## PENTOTHAL® Sodium

(Thiopental Sodium, Abbott)

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## *When you think of Sutures, think of –*

# DEKNATEL

**STERILE PACKED:**

- READI-CUT SILK AND COTTON, dry pack
- SURGICAL GUT

**NON-STERILE:**

- SPOOLED SILK, COTTON AND NYLON
- READI-CUT SILK AND COTTON
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DEKNATEL Stainless Steel MTN (Minimal Trauma Needles) can be supplied swaged on all sutures.

Their high temper, sharp points and keen cutting edges minimize tissue reaction, give maximal resistance to bending or snapping. Stainless steel eliminates the rust problem in the dry pack.

***Do you require a needle especially designed for a new technique?***

***Minimal Trauma Needles are manufactured in our own plant. The DEKNATEL Research Staff can make any needle to your specifications.***

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J. A. DEKNATEL & SON INC.

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# Meat...

## *Dietary Cholesterol and Vascular Sclerosis*

Recent studies reaffirm the "hypothesis that atherosclerosis is fundamentally a metabolic disease subject to important dietary influences"[1] and do much to refute contentions that foods containing cholesterol should be avoided in general diets.

Arterial disease resembling that in human subjects was produced in Cebus monkeys fed diets high in cholesterol and low in sulfur amino acids. Within 2 to 8 weeks after initiation of the regimen serum concentration of cholesterol rose to levels of 300 to 800 mg. per 100 ml. "The hypercholesterolemia could be largely prevented by feeding 1 gram per day of dl-methionine or l-cystine as supplements to the diet." Also, the elevated cholesterol levels "could be restored to normal by feeding 1 gram of dl-methionine but only partially restored by 0.5 gram of l-cystine daily."

According to the investigators, the "vascular lesions were in the ascending aorta but extended from the valves of the left ventricle to the proximal portions of the carotid and femoral arteries . . . The aortic lesions were chiefly characterized by the presence of lipid-laden phagocytes and increase in collagen and elastic fibers. The lipids were in part cholesterol derivatives."

Cholesterol, an essential metabolite produced in intermediary metabolism,[2] is biosynthesized from dietary protein, fat, and carbohydrate.[3] Normally, its synthesis is exquisitely controlled to insure adequacy as well as to protect against an oversupply.[4] Furthermore, considerable evidence indicates that an increased cholesterol intake is not an etiologic factor in alleged aberrations of cholesterol metabolism such as atherosclerosis.

In widely variable amounts, cholesterol occurs in foods of animal origin—meat, poultry, fish and marine foods, eggs, milk products—all foods of great nutritive value.[3] Present knowledge in no way warrants alteration in the customary consumption of these foods because of their contained cholesterol.

Skeletal muscle of beef, lamb, pork, and veal provides but small amounts of cholesterol, approximately 0.06 Gm. per 100 Gm. moist weight of meat.[5] Since atherosclerosis may interfere sharply with normal nutrition, the patient should consume diets rich in protein foods (such as meat), vitamins, and fruit.[6] In addition to high quality protein, meat supplies valuable amounts of needed B vitamins and essential minerals.


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**American Meat Institute**

**Main Office, Chicago...Members Throughout the United States**

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## COLOR CODED

TRADE MARK PAT. APPLIED FOR

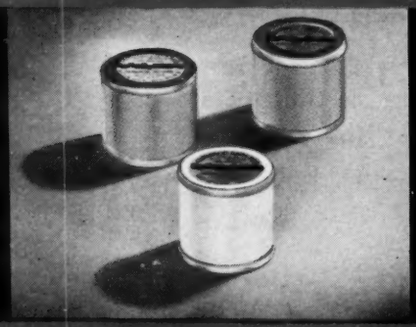
## SUTURES

4-0 PINK 3-0 BLUE 00 WHITE

Correct size suture is immediately selected when the ORN supplies Gudebrod COLOR CODED—no hesitation, never a question.

*An exclusive GUDEBROD feature* SURE AS A FINGERPRINT

Available in CHAMPION serum-proof silk or HAND-CRAFT cotton



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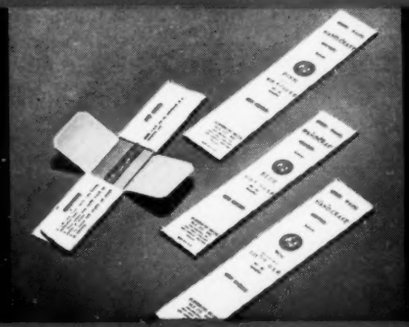

GUDE-PACK

DRI-PAK®

Gantrisin / 'Roche' a single, soluble, wide-spectrum sulfonamide

tablets, pediatric suspension, syrup, ampuls, ophthalmic solution and ointment.

## Pneumonia*

℞ Gantrisin tabs. 0.5 Gm

#60

S. 8 tabs. initially; then

4 tabs. q. 6 h., p.r.n.

## Meningitis*

℞ Inject i.v. 10 cc (4 Gm)

Gantrisin Diethanolamine q. 8 h.;

then shift to oral medication

with 4 tabs. (2 Gm) q. 6 h.

## Tonsillitis* in child weighing 40 lbs.

℞ Gantrisin (acetyl) Pediatric

Suspension ℥ iv

S. Initial dose 2 teasp.; then

1 teasp. q. 6 h.

## Urinary infections*

℞ Gantrisin tabs. 0.5 Gm

#100

S. 8 tabs. initially; then 4

tabs. q. 6 h., p.r.n.

## Cystitis* in child weighing 40 lbs.

℞ Gantrisin (acetyl) Syrup ℥ iv

S. Initial dose 2 teasp.; then

1 teasp. q. 6 h.

## Blepharitis*

℞ Gantrisin Diethanolamine

Ophthalmic Ointment 4%, 1/8 oz

S. Use in eye 3 times

a day and at bedtime

* ... when due to streptococci, staphylococci, meningococci, H. influenzae, K. pneumoniae, E. coli, B. proteus, B. pyocyaneus (Pseudomonas aeruginosa), A. aerogenes, paracolon or alcaligenes fecalis. As is true of all antibacterial agents, there may be failures due to resistant strains.

Gantrisin® - brand of sulfisoxazole (3,4-dimethyl 5-sulfanilamido-isoxazole)

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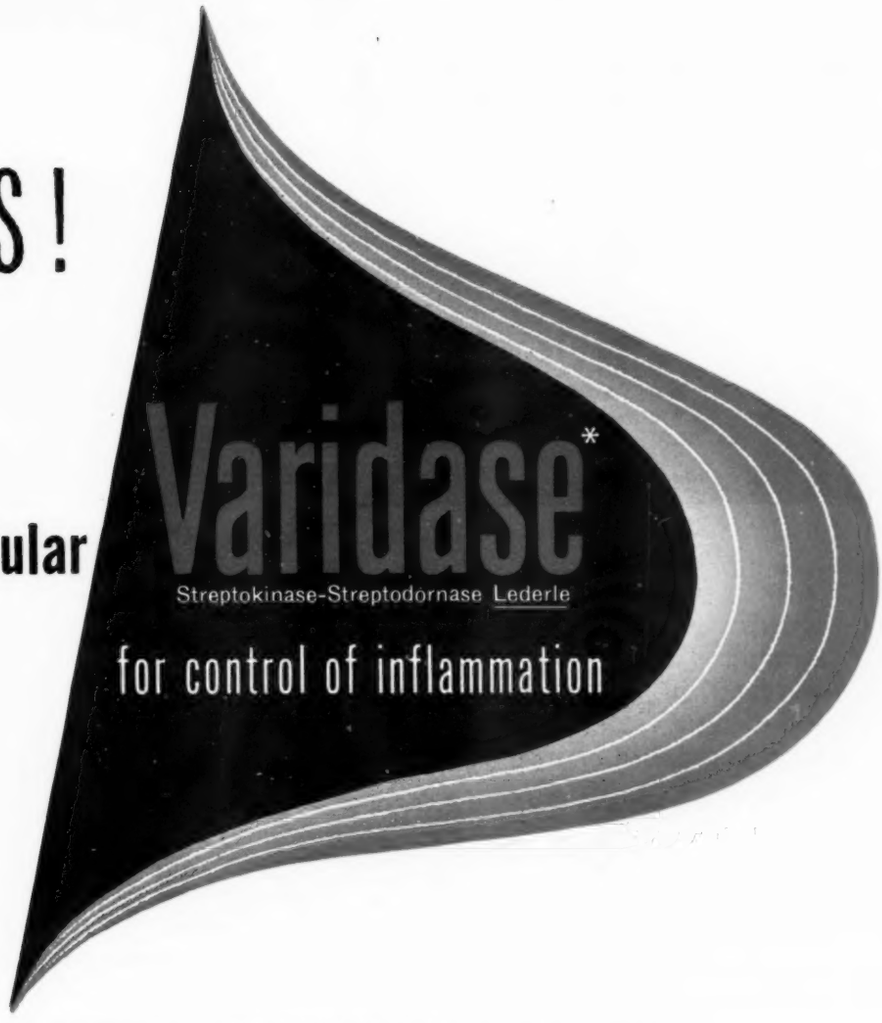
# NEWS!

## intramuscular




Injected intramuscularly, VARIDASE has produced remarkable results in the treatment of abscess, cellulitis, edema, epididymitis, hemarthrosis, sinusitis and thrombophlebitis with or without superimposed infection.

VARIDASE quickly dissipates simple inflammation. In treating infected lesions, antibiotics should be administered concomitantly. In such cases VARIDASE breaks down the "limiting membrane" which contains the infection, allowing passage of the antibiotic.

**TOPICAL USE**

VARIDASE dissolves clotted blood and pus, promotes growth of healthy granulation tissue. Applied topically or instilled; in solution or jelly form.

Available in three forms:

1. 20,000 units streptokinase and 5,000 units streptodornase.
2. 100,000 units streptokinase and 25,000 units streptodornase.
3. Special combination package consisting of 100,000 units streptokinase and 25,000 units streptodornase with jar of 15 cc. Carboxymethylcellulose jelly.

LEDERLE LABORATORIES DIVISION *AMERICAN Cyanamid COMPANY* Pearl River, New York

Lederle

*REG. U.S. PAT. OFF.

# Enriched Bread in Special Diets

THE many advantages of enriched bread in special diets are all too seldom recognized or appreciated. Hence, the physical, physiologic, nutritional, and dietetic values of enriched bread warrant detailed enumeration.

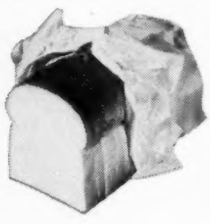
The open, soft texture of enriched bread enables its easy mastication, its ready absorption of digestive juices, and its prompt and thorough digestion. Reflexly, its appetizing eating qualities enhance the digestive processes. Since bread is free from coarse or harsh vegetable fiber, it proves nonirritating mechanically to the gastric and intestinal mucosa. In metabolism its minerals are neutral.

Enriched bread contains less than 0.2 per cent fibrous material, yielding insignificant amounts of indigestible residue. It contains only 3 per cent of fat, negligible amounts of purines, no cholesterol, and does not interfere with the digestive or absorptive processes. It contributes to a desirable texture of the food mass throughout the intestine. The contained nutrients are absorbed gradually.

Nutritionally, enriched bread supplies valuable amounts of biologically valuable protein, 8.5 per cent; easily digestible carbohydrate, essentially starch and dextrins, 52 per cent; and minerals, 1.8 per cent. Enriched bread provides notable amounts of vitamins and minerals: each 100 grams supplies on the average 0.24 mg. of thiamine, 0.15 mg. of riboflavin, 2.2 mg. of niacin, 88 mg. of calcium, 92 mg. of phosphorus, and 2.6 mg. of iron. Also it provides 275 calories of nutrient energy per 100 grams.

Enriched bread, in either fresh or toasted form, contributes to the eating pleasure of many other nutritious foods. Its neutral flavor permits it to blend well with other foods.

For these reasons, enriched bread enjoys a prominent place in a great variety of special diets—soft, low residue, low purine or cholesterol diets, general hospital diets, as well as diets low or high in carbohydrates, in proteins, or in calories.



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**AMERICAN BAKERS ASSOCIATION**
20 NORTH WACKER DRIVE • CHICAGO 6, ILLINOIS

# new drying agent

*for preanesthetic medication*

# Antrenyl®

## Injectable Solution

. . . decreases salivary, pharyngeal and respiratory secretions

. . . "superior . . . to either atropine or scopolamine . . ."[1]

. . . prolonged drying effect—lasts 3 to 5 hours

. . . minimum postoperative nausea and vomiting—no urinary distress

. . . for all age groups and all types of surgery

*Supplied:*

Multiple-dose Vials, 10 ml., each ml. containing 2 mg. Antrenyl bromide.

1. Stephen, C. R.: Personal communication.

Antrenyl® bromide (oxyphenonium bromide CIBA)

C I B A

SUMMIT, N. J.

2/2117M

# Primum Non Nocere

The primary concern of the dermatologist is embodied in the dictum, "Primum Non Nocere," meaning "*First do no harm.*"[1,2]

A major attribute of Desitin Ointment is its non-sensitizing, non-irritant, non-toxic[4-6] quality even when applied over extensive, raw skin areas. To soothe, protect, lubricate, and accelerate healing ... without causing "therapeutic" or "overtreatment" dermatitis ... rely on

# DESITIN®

## OINTMENT

*rich in* **cod liver oil**

*in* **diaper rash • wounds** (especially slow healing)
**ulcers** (decubitus, varicose, diabetic) **• burns**
**dermatoses • rectal irritation**

**Tubes of 1 oz., 2 oz., 4 oz., and 1 lb. jars.**

*May we send* **samples** *and literature?*

**DESITIN** CHEMICAL COMPANY • 70 Ship Street, Providence 2, R.I.

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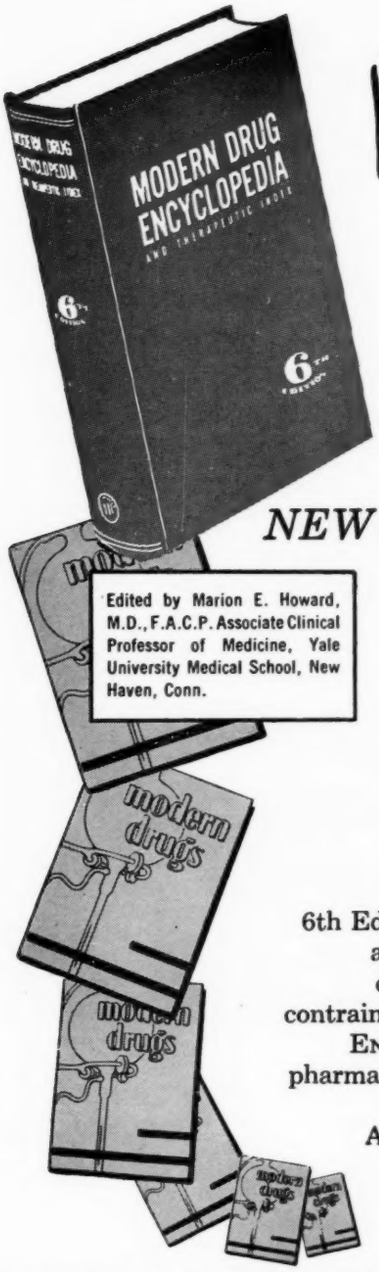


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VOL. 89 JUNE 1955 NUMBER SIX

# Emile F. Holman, M.D.

LOREN R. CHANDLER, M.D., *San Francisco, California*

BECAUSE of recurring birthdays and University rules Emile F. Holman will be promoted to Professor Emeritus at Stanford University School of Medicine at the end of the present academic year. Our Medical School loses much because of his removal from undergraduate teaching and day-to-day supervision of our Surgical Department. To the rest of the medical profession and the public, however, he will still be available because he intends to carry on much of his non-academic work.

Emile Holman is great as a surgeon, teacher and investigator. His greatness is evidenced by the more than twenty-five academic honors and positions which he has held; his membership in a long list of distinguished scientific societies, nine of which have honored him with the Presidency; and his selection as winner of the Samuel D. Gross prize, the Rudolf Matas Award in Vascular Surgery and as recipient of the Medaille de Roi Albert. His list of publications, both books and scientific articles, is long and distinguished, beginning in 1919 and continuing with increasing importance and volume to the present time. Emile has pioneered in studies and is a recognized world leader in knowledge of arteriovenous fistula, aneurysm, surgery of congenital heart disease, poststenotic dilatation of vessels and, indeed, several other fundamental investigations which have been repeated by others and accepted by everyone.

Emile returned to Stanford University in 1925, having received his A.B. degree here in 1911. In 1926 he was appointed Professor of Surgery and Executive of the Department in the School of Medicine. His exceptional academic background, which besides Stanford includes experience at Oxford, Johns Hopkins, Harvard and Western Reserve School of Medicine before he came to our medical school, made him eminently qualified to launch a long-term program for better teaching and training of undergraduates as well as graduates in his department. He began quietly but with skill and determination to expand and improve surgical training. The research laboratory for the department was enlarged and its activities promptly increased. The resident training program was expanded and experimental surgery made a part thereof. Students, interns, residents and fellows "learned by doing" under his superior direction. He and his department attracted candidates with unusual ability. During the twenty-nine years which he has led us in surgery, an impressive group of distinguished surgeons has been developed and matured by him.

As a teacher Emile is dynamic, specific and at times a little dramatic if it will emphasize a point. His knowledge of the scientific literature seems to be boundless. He is always available, never too busy to consult and confer with associates or assistants, and he is a slave for

work. Meticulous and exacting in his technics, he is never more critical or demanding of others than he is of himself and he has been a leading example of humanitarianism in his clinical work.

We at Stanford who lose him as our leader are grateful for this association and the privilege of having worked for and with him over these years, because each of us is vastly richer for the experience. We have a deep appreciation as well as a great admiration and all of us, Emile, *Salute You.*

# A
# COMMEMORATIVE ISSUE

DEDICATED TO

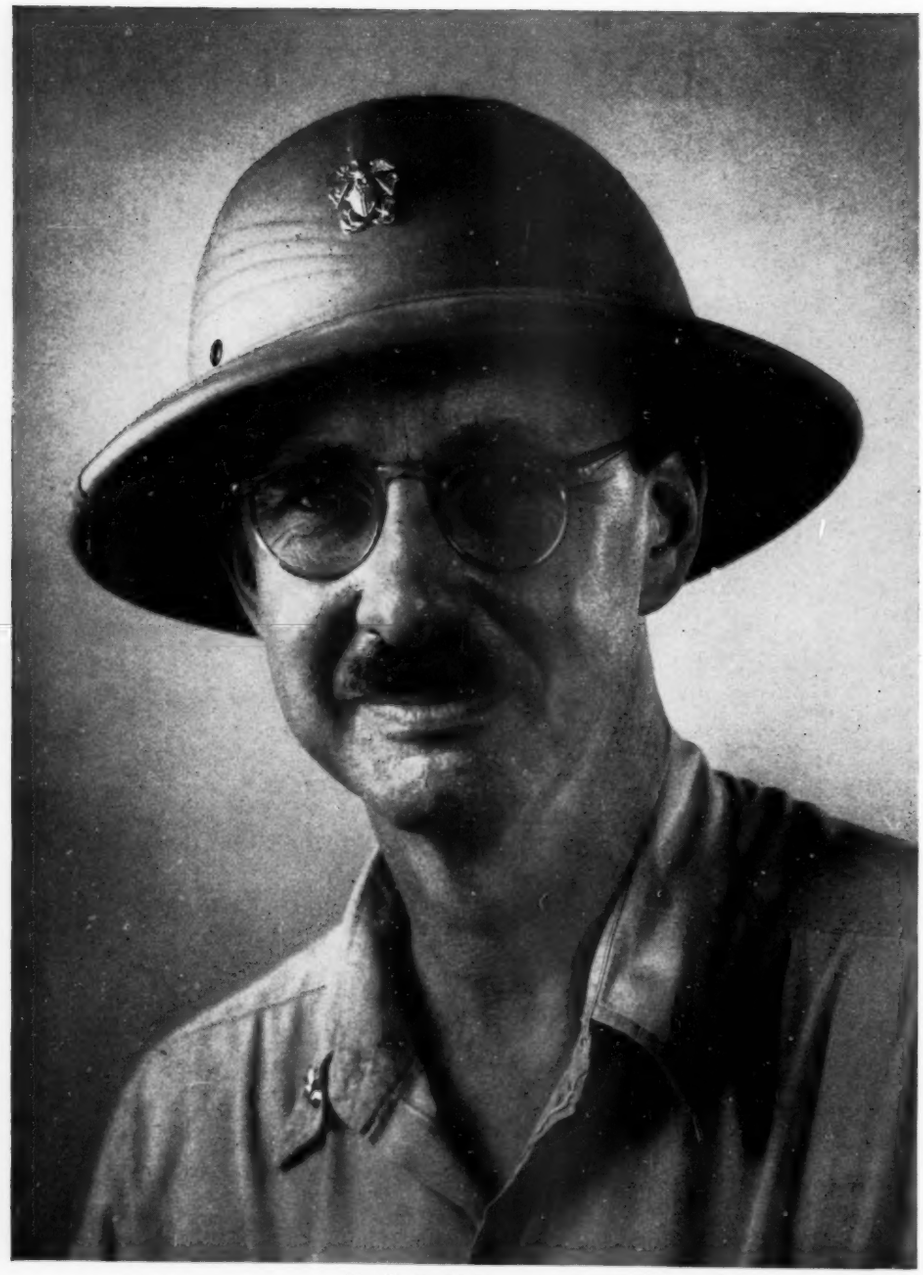
EMILE F. HOLMAN, M.D.

*Guest Editor*

VICTOR RICHARDS, M.D.

THE AMERICAN JOURNAL OF SURGERY, INC.

*June* 1955 *Issue*



Emile F. Holman, M.D.

# A Tribute

OTHERS may tell (1) of a competent organizer; (2) of an astute surgeon of unusual skill who was also a scholar; (3) of a teacher, great by precept and by example; (4) of an imaginative, tireless and incredibly enthusiastic investigator; (5) of a jauntily defiant dissenter from established medical traditions, who believed so firmly in the fundamental truths he could demonstrate in his experiments that he took on and sometimes routed in their own fields such doughty adversaries as Sir Thomas Lewis and Dr. Maude Abbott (in these battles his head was often bloody but never bowed).

But few may know and none may speak of his service "beyond the call of duty." The teacher within him driven by the desire to be with and to help the young front line casualty surgeons he had trained, and the investigator within him constantly driven by John Hunter's urge, "Do not theorize; try it and see," impelled Stanford's over-aged Professor to squeeze under the line into the Navy. After a very checkered service, ranging from surgical intern to surgical chief at Mare Island base hospital, he was shipped out to the Pacific Theatre of war and sent north with the Marines to Vella La Vella. There he organized the Jungle Island Medical School and in its crude Hunterian experimental laboratory, under his experienced eye, young surgeons who had been medically idle for almost a year again practiced their surgical skills. There the Professor himself pursued his investigations into better methods of wound healing on wild dogs purchased from the natives at exorbitant prices paid from his own pocket.

There and in his other assignments he introduced ward rounds and gathered together all the doctors from near-by services for bedside teaching and pooling of the often scant clinical material available to scientific men while they marked time at their battle stations before the push began.

Always impelled by an inextinguishable urge to test at first hand the principles he had conceived in the security of a base hospital, he constantly pleaded to be sent further forward. Finally he was permitted to establish on Pellilieu his operating room within 500 yards of the front line and to evacuate, directly, the fresh casualties from the Tinian beaches under Bloody Nose Ridge.

To these and other little-known extracurricular acts of courage and dedication I bear witness and pay tribute.

ANN PURDY, M.D.,
*San Francisco, California*

# The Brigham in Emile Holman's Day

FRANCIS D. MOORE, M.D., *Boston, Massachusetts*

ON July 15, 1923, Emile Holman began his work as Assistant Resident in Surgery at the Peter Bent Brigham Hospital. Prior to his arrival at the Brigham Dr. Holman had already worked at many institutions, including Stanford where he had received his A.B. in 1911, and Oxford, with periods spent at the Royal College of Surgeons in Edinburgh, the Rotunda Hospital in Dublin and the National Hospital in London. He had received his M.D. from Johns Hopkins in 1918 and, after a period of time in the Children's Hospital there, had been Assistant Resident in Surgery from 1919 to 1923. He was therefore an accomplished surgical traveler even before his Residency; many former friends and associates from Johns Hopkins as well as former teachers were already at work at the Brigham when he arrived on that July day thirty-two years ago. It is the purpose of this article to evoke a little of the atmosphere and to recall something of the people who were at the Brigham during Emile Holman's time as Assistant Resident and then Resident in Surgery.

When he arrived at the Brigham, the hospital was ten years old. It had been opened in 1913 after a four-year period of construction and after a twenty-five year period during which the original Brigham legacy had been held in trust to accumulate interest. Brigham architecture was at that time still "in the the raw." The Brigham architect has often been referred to as a man who never spent a winter in New England. Whether it was this ignorance of local climatic conditions or his enthusiasm for fresh air has never been known; whatever the motive, he built the hospital as a series of unconnected wards with open-air passages between. The "pavilion" system of hospital architecture was based on the concept that if pestilence started in one ward, the others could be isolated. This scheme of architecture became obsolete in this country at about the time the Brigham was opened. It has taken four decades to restore to a functional pattern the theoretic concepts of this architect.

The Brigham architecture and its funded wealth were untouched at that time. At its opening it is said that the Brigham was the richest hospital in the world, by which was meant that it had more capital investment per bed than any other hospital. The ravages of the middle thirties had not yet occurred. These were ravages which were to rob the Brigham of much of its capital and most of its securities income, converting it by stages (along with many other hospitals in this country) to its present penurious status with all the faults and virtues of struggle and poverty. However, in 1923 the Brigham was rich; medical school budgets were virtually unheard of and the research grant had not yet been invented. Prior to the opening of the hospital the two clinical chiefs, Dr. Cushing in Surgery and Dr. Christian in Medicine, together with some of their staff, had traveled in Europe and had gathered some of the atmosphere of the European centers with which they were already familiar from previous study.

The Brigham was a new phenomenon in Boston for three reasons. First, it was built adjacent to the Harvard Medical School which had been moved to its Longwood Avenue quadrangle in 1906, and it was conceived as a hospital very close to the University in its objectives. Second, it had been founded on a "full time" system, yet one which varied in degree from the "pure full time" system embodied in the Johns Hopkins faculty arrangements. Third, the hospital traced its intellectual ancestry chiefly to Johns Hopkins and only secondarily to the Massachusetts General. The chiefs of staff and many of their lieutenants had received their medical education at Johns Hopkins. Dr. Cushing in his pre–Johns Hopkins days had been a house pupil at the Massachusetts General Hospital in 1895 after graduating from Harvard Medical School. Dr. Homans also had an ancestry involving both the Harvard–Massachusetts General Hospital background and Johns Hopkins. Dr. Cheever was exclusively a Harvardian, with

clinical experience at the Boston City Hospital.

At the time of its opening the Brigham laid the groundwork for its future growth with great care. Arrangements for research were developed very early. The teaching of students played a part in the life of the hospital from the day of its opening, and its service to the community was carefully documented not only in a very complete record system but also in a detailed analysis each year of the patients seen and the care that they had received.

On his arrival Dr. Holman found himself working under Dr. Daniel Elkin, who at that time was Resident. After a three-month period Dr. Elkin had to leave because of illness in his family and Dr. Holman took over the position as Chief Resident. Dr. Cushing writes in his report: "Dr. Elkin in turn was succeeded on September 1st by Dr. Emile Holman who had been for two years Professor Halsted's Resident on the Surgical Service at the Johns Hopkins Hospital. It was fortunate for us that a man of his training and ability could have been available to step into the gap left by Dr. Elkin's early resignation from the position, for it is most desirable that the traditions of the post be handed on without any conspicuous break in the sequence."

Dr. Holman in turn held the post until the following July, his period as Resident falling somewhat short of the year or two which was the rule at that time.

During his Residency Dr. Holman found time to work in the laboratory in Building C of the Medical School, a laboratory founded through the foresightedness of Dr. J. Collins Warren and functioning since 1909. In the laboratory Dr. Holman studied with Dr. Merle Scott and Dr. Claude Beck. Much of his early work had to do with arteriovenous fistula and surgery of the heart. It is prophetic that Dr. Cushing should write in his 1924 report as follows: "The last two appointees, Dr. Scott and Dr. Beck, who as the Arthur Tracy Fellows have been in charge of the laboratory, have both done excellent work and a number of the hospital staff have managed to carry to this laboratory certain problems deserving of investigation. Among them, I may especially name Dr. Holman, who has found time to pursue his studies on the consequences of arteriovenous fistula, a subject with which he had already identified himself before joining our staff. During his term, Dr. Scott made some valuable additions to our knowledge of the relation of the adrenal glands to infection; and Dr. Beck has largely been engaged during the fall semester assisting Dr. Cutler in his experiments concerned with the future operative surgery of cardiac derangements. It is to the great credit of the Brigham Hospital that the first successful operation for mitral stenosis to be recorded has been the outcome of this work. Unless all signs fail, we are on the eve of a new surgical specialty of great promise—a specialty dealing with the chronic disorders of the heart. The subject, however, is one in which haste must be made slowly."

Dr. Cushing's enthusiasm at seeing this field of surgery develop was a natural one not only because of his pioneering instincts but also because he realized acutely that the Brigham Hospital at that time tended to marshall an unbalanced segment of human disease, with much too great a representation from disorders of the central nervous system, particularly brain tumors. During this period the great upswing in Dr. Cushing's neurosurgical practice was just beginning and was to reach its peak during the subsequent six or seven years. At its peak almost 40 per cent of the surgery carried out at the Brigham was neurosurgery, and a great majority of the men on the staff were later to make their mark in this field. This was a natural development with a staff under the leadership of the world's foremost neurosurgeon, but Dr. Cushing realized the hazards involved and welcomed this new development with enthusiasm.

During his year as Resident Dr. Holman performed the great majority of the surgery on the service. The House Staff was small, only two or three interns or assistant residents being appointed each year. The volume of surgery was not great, amounting to approximately 1,800 operations or approximately two-thirds of the current volume with the same bed capacity. The pace was leisurely and there was time not only for research but also for other pleasurable activities.

Dr. Holman's publications from this period bespeak the intensity of his interest and the amount of time available to the Resident for investigative work. He published five papers, most of them originating from work carried out at the Brigham but with roots going back to his previous experience.

FIG. 1. Dr. Emile F. Holman is fourth from the right in the back row. Dr. J. Collins Warren is holding his derby hat, sitting in the center of the second row. The rest of this row is, from left to right, Dr. Sosman, Dr. Homans, Sir D'Arcy Power, Dr. Cushing, Dr. Christian, Dr. Cheever, Dr. Fitz, Dr. Quinby and Dr. Frothingham. Others in the picture are identified in the text.

To see who was there at the Brigham with Emile Holman, let us take a look at the staff picture taken in April or May, 1924. (Fig. 1.) This is a picture of both the Medical and Surgical Staffs, with representatives also from Pathology and Radiology. It shows, sitting in the middle of the second row, Dr. J. Collins Warren who had been the first Moseley Professor (from 1899 to 1907) and who had founded the laboratories in Building C.

Dr. Merrill Sosman was one of the men whose later work was chiefly at the Brigham or in Boston. At that time he was by far the youngest on the staff to have departmental responsibility. Immediately behind him is Dr. Elliott Cutler who was to leave the following year, taking Drs. Holman, Scott, Beck, Joelson (one of Dr. Quinby's pupils) and Harbin with him to Western Reserve in Cleveland. The Brigham was subject to periodic "housecleaning" in this form when individuals left the staff to take up professorial posts elsewhere and took a number of their associates with them.

Standing behind Dr. Christian is Dr. Samuel Levine, cardiologist. Drs. John Homans,* David Cheever, Channing Frothingham, Clifford Derick and Sir D'Arcy Power are all in the picture as well as Dr. Fletcher Colby who was to return to the Massachusetts General Hospital after his time with Dr. Quinby and ultimately become the Chief of the Urological Service there.

* According to Dr. Sosman, there was one individual for whom Emile Holman's Boston stay was a major inconvenience. This was John Homans, whose daily life was complicated by Emile Holman's presence because the two names were so similar. The telephone operators, the mail-sorting desk, the messages sent to the wards, hurry calls from the operating room and social invitations were commonly confused between the two. John Homans was always spluttering, muttering, coughing and cussing about it. Sad though it is to relate, John Homans was greatly relieved when Emile Holman left for Cleveland.

Of men who were to leave the Brigham and achieve eminence elsewhere are seen Dr. William Dock, later to become Professor of Medicine at New York University, and Dr. Loyal Davis, who took the neurosurgical training he gained with Dr. Cushing to return to Chicago as professor at Northwestern. Drs. Tracy Putnam, Merle Scott, Cyrus Sturgis, Claude Beck and Gilbert Horrax are all prominent in the picture. Dr. Norman Dott, who was to return as Chief of Neurosurgery at Edinburgh, is standing behind Dr. Warren. Of course Drs. Quinby and Reginald Fitz were there.

There were various other members of the staff that year who do not appear in the picture, including Drs. Glen Spurling and Cornelius Rhoads as well as James Paterson Ross, who was at the Brigham studying under Dr. Cushing and was later to return to St. Bartholomew's Hospital in London as Professor of Surgery. As the years went by, Dr. Emile Holman was to come back to the Brigham as Surgeon-in-Chief Pro Tem in 1951, to be followed two years later by Sir James Paterson Ross as the Pro Tem in 1953. Drs. Francis Peabody and Burt Wolbach are not in the photograph, nor are certain of the consultants who spent a good deal of time at the hospital, including Drs. Hans Zinsser, Walter Cannon and Otto Folin, all of whom occupied positions of responsibility as chiefs of preclinical departments in the Medical School.

Although the Brigham had been set up with a "full time" system, it had immediately adopted the pattern which has now come to be characteristic of Harvard faculty arrangements; namely, that the full time chiefs of clinical services received an institutional salary from the Medical School and the University combined but in addition were allowed some private practice, the amount of this practice being settled wholly by a gentlemen's agreement that they would not become unduly preoccupied with it. In spite of the fact that this system had been in force for ten years, it was still a source of much puzzling and soul-searching on the part of Dr. Cushing. The Brigham had facilities for a few private patients at that time but the members of the staff did not have "offices." That term must have been considered a word of opprobrium. Instead they had "consulting rooms." These consulting rooms were the places where they saw their private patients. They were used increasingly for study, for centralization of effort, for teaching students and for all the other purposes to which a hospital professional office is put.

Because of the continuing prominence of this problem in the organizational patterns for surgical service throughout this country, it is possibly of interest to quote in some detail Dr. Cushing's thoughts, written in 1924: "Meanwhile, another and more rigid form of full time service has been adopted in a few other institutions, primarily at the Johns Hopkins where ten years ago the matter was first being agitated. On this other basis, larger salaries were given but the incumbents were supposed to be protected against the temptations of having private work interfere too greatly with their hospital duties by having the institution charge and collect the professional fees from private patients. These fees were to be wholly or in part turned back to the department concerned, or, in some cases, even added to the general funds of the hospital or of the university.

"With either system, abuses may occur. A university hospital having under contract a full paid surgeon and at the same time a private pavilion whose occupants are charged fees, may bring unjustifiable pressure upon him to attend patients and to operate for conditions in which he may happen to be academically uninterested; for he is supposedly a teacher and investigator and may be engaged in problems he does not wish to interrupt. This applies no less to the physician than the surgeon, but is particularly hard on the latter in view of the time-consuming nature of the therapeutic procedures he may be called upon to perform. . . . On the other hand, a hospital attendant who at the same time holds an academic post, be he physician or surgeon, may become so engrossed in his personal affairs that he neglects his hospital and academic duties. . . . If an attendant so prostitutes his position, and the governing bodies of the school and hospital cannot make him see the light, he had much better be promptly superseded. A personal element, of course, enters into all these relationships. One man's meat is another man's poison. The same formula does not fit different personalities. . . . And there can be no doubt but that under certain circumstances hospital attendants may come to ignore the humanitarian side of medicine and

to look upon the patients on the wards as so much material to be disposed of. . . . Those of us who saw much of the service in Army Hospitals, where medical officers were under contract to do the government's work and otherwise had no personal responsibility for the patient's welfare, realize perhaps better than others the hardening influence of this kind of relationship even to the most conscientious officers."

Dr. Holman, then, found himself in a young institution which was rather self-conscious of its position with relation to the many other university hospitals which were at that time starting their evolution in this country. It was a hospital where research and teaching occupied a high position in a man's consciousness. Fundamental biologic investigation was taken for granted as a part of surgical growth and we had not yet developed self-styled experts who decried "superscience" in surgery and seemed to be groping for some sort of makeshift substitute. It was a time when the pace of clinical work was such that the Assistant Resident could easily pursue fruitful investigations while still attending to his duties on the wards. It was a hospital where the private practice of surgery had a secondary role, although the Chief of Surgery very rightly called attention to its importance in sharpening the wits and conscience of the medical or surgical teacher.

This was also a period when literary activity was at a high tempo. It is of interest that in the Annual Report for 1922, 1923 and 1924, Dr. Cushing notes nothing of his own literary activity. In the bibliography for 1925 we see a single reference to "The Life of Sir William Osler. The Clarendon Press, Oxford. Two Volumes. 1925." This great work, for which the author was to receive the Pulitzer prize and to which he devoted great time and effort, was written on nights, Sundays and holidays while traveling and often at his home on Walnut Street. Sunday mornings at the Walnut Street house were a time of study and writing for the Chief, and the Resident Surgeon frequently came out there at that time to talk with him about patients or research problems and in so doing saw Dr. Cushing in the midst of his literary and creative efforts.

We can close our little retrospective picture with a sunny May morning in Brookline in 1924, when Drs. Cutler, Beck and Holman called on Dr. Cushing as he worked. They talked with him about the patients they had seen, and planned with him their first adventures into the surgery of the heart and great vessels. Drs. Cutler and Beck soon left for Cleveland where Dr. Cutler became immersed in departmental organization and Dr. Beck carried forward his interest in cardiovascular surgery. Dr. Holman shortly thereafter returned from Cleveland to his home in California where in 1926 he became Professor of Surgery at Stanford. As mentioned heretofore, he returned to us in 1951 for a visit as our "Pro Tem," bringing back to the Brigham the warmth of his personality, the keenness of his perception and his enthusiasm for teaching surgery. The Chief, Dr. Cushing, worked ten more years at the Brigham before he retired, returning to his Alma Mater in New Haven to round out his career of great contributions to American letters, to the field of neurosurgery, but above all to our understanding of pituitary endocrinology, the field which history will assign to him as the first great American pioneer.

Looking back, those seem like leisurely days. The many men still on our staff remember them also as days when things were done slowly and with great care. There was always an eye to future meanings and a sense of intense personal responsibility for future developments in medicine and surgery. This was an atmosphere which is hard to recall in bustling 1955 but it is one which should be recalled because it embodies many ideals toward which we can all strive.

EDITORIAL

# A Patient or a Case

GEORGE D. BROWN, M.D., *Pomona, California*

IN times like these, when men of the caliber of Dr. Holman have made such tremendous advances in surgical technics, it distresses me to see a strained relationship developing between many doctors and their patients. This situation is brought to our attention in several ways: a growing demand by the public for socialized medicine, a demand for the profession to come to an agreement on some fixed fee schedule, and the necessity for county societies to establish a complaint committee to judge and arbitrate disagreements between members of the society and their patients.

A glance at these public demands would indicate that many people believe they are unable to obtain good medical care, a necessity of life, for a price they can afford to pay. The problem of payment for medical care is not a new one; it has always been with us. In the past the solution to this problem has been a very close relationship between the doctor and his patient. The closer the relationship, the smaller the problem. Our pioneer physicians had one goal uppermost in their minds when called on for service and that was proper diagnosis and restoration of the patient to health. Payment for that service was a secondary consideration. In many cases their reward was not in dollars.

These old physicians knew each patient not only as an individual with an illness which required medical or surgical care, but also as an individual with social and economic problems common to all of us. He also realized that this patient had the same hopes and desires for his family that physicians have.

When a statement for services was rendered, this doctor not only had considered the time and skill required to restore his patient to health, but also had considered the patient's social and economic status and had sent a statement which he considered fair to all concerned. It was a rare case indeed which would require the deliberation of a complaint committee. This doctor had a patient who respected him and was deeply grateful to him for the services which had restored him to health. Most likely the doctor's reward in dollars would be considered inadequate if it were possible to place an actual dollar value on his services. However, the doctor had received a very tangible reward in seeing his patient restored to health or relieved of his suffering. He received still another reward from the knowledge that in the charge for his services he had made it possible for the patient's family to live their lives free of burdensome debt.

It seems to me, as we gain more scientific facts, that the trend in medicine is toward the loss of much of our ideology and art. We are apt to consider only the scientific aspects of an individual case from a diagnostic and therapeutic standpoint and to disregard the economic and social problems which confront the individual. When we do this, we are treating a "case" and not a "patient." I am sure it is this situation which is the basis for many of the strained relations between doctor and patient.

I do not believe socialized medicine is the answer to our problem. I am very sincere in the belief it would reduce our present high standard of medical care. I do not believe standard fee schedules are the answer. Who can place a cash value on life? Who can place a cash value on services designed to preserve it? I cannot. I can place a value on my services which will make it possible for me to live in reasonable comfort and at the same time allow my patients to live in a similar manner.

Perhaps we have gone too far already; yet I cannot help but think that if we mix enough of our old ideology with present scientific ad-

vances and make "patients" out of "cases," it will do a great deal toward solving many of the problems which confront the profession today.

It seems to me it would be difficult to get a patient who is grateful for what you have done for him and appreciative of the fact that you have asked a payment which he could afford, to go to a state- or government-sponsored clinic where he must receive a case number and consult a physician not of his choosing.

I do not believe a patient would choose to pay a "standard fee" of $400.00 for a service for which, under his circumstances, you would ordinarily charge $100.00. The only group who would favor this is the group in which there is no problem of adequate medical care today.

It would be much more difficult for some of our ill advised legal friends to convince an individual whom you had treated as a "patient" rather than a "case" that there is "easy money" to be obtained from a malpractice suit against you.

I believe that if monetary wealth is our goal we should be engaged in some commercial enterprise, not involved with the necessities of life and not in the humanitarian profession of medicine.

I am sure our problems will not be solved by some federal, state or society edict. We must solve them as individuals and as members of a profession which is based on service to our fellow man.

Who could be wealthier than Sir Alexander Fleming in the gratitude he has received for his discovery of penicillin; yet his monetary reward was a mere pittance for his service.

I have found in the past and still find that a large majority of the people I treat are honest, ambitious citizens who, when treated as "patients" instead of "cases" are loyal, grateful and appreciative patients not clamoring for some new method of obtaining medical care. When a statement for services is sent, you will receive your monetary reward; and so many times there will be an accompanying note of appreciation for the services rendered. On the latter you pay no income tax. Frequently, however, to be commercial, its financial value is much greater than suspected. In the United States there are no class barriers and many fine people of modest incomes claim as their closest friends people with very high Dunn and Bradstreet ratings.

I sincerely believe the only satisfactory and happy solution to our present day problems in medical practice is to make more "patients" out of "cases." If we do not, some Government agency will make "cases" out of all of our "patients."

May I pay the highest tribute to the man whose tolerance of my early efforts and confidence in my ability has made it possible for me to bring health and comfort to many families. I cannot pay him in money for the service he gave me, but I and my patients are grateful to Emile Holman.

# The Physiology of an Arteriovenous Fistula*

EMILE HOLMAN, M.D.

CARDIAC hypertrophy and proximal dilatation of the artery have been so frequently associated with arteriovenous fistulas that it has long seemed highly probable that there must be some causative relationship between the two. That such a relation exists has been denied by clinicians, both ancient and modern, and the association of the two conditions clinically has been attributed to a coincidence. It was a problem that aroused the interest of the late Professor Halsted many years ago, and was for him a subject of constant speculation. Speaking before the American Surgical Assotion[1] in 1918, he said:

"If the assumption is correct that the heart dilates in consequence of the fistula, it is important that the fact should be brought to the attention not only of surgeons but also of pathologists and internists who apparently have altogether overlooked it . . . When a causative relationship . . . shall have become convincingly established, we may find that some unexplained dilations of the heart are referable to hitherto undetected changes in the walls and lumen of the blood vessels."

Dr. Halsted's interest in the subject prompted him to collect all the clinical evidence bearing on the subject in the 447 arteriovenous fistulas of the larger vessels recorded in the medical literature of the world. These data, published by Dr. Curle L. Callander,[2] make an absorbingly interesting story of a comparatively rare clinical picture. The article carries an excellent bibliography.

Among these 447 cases, there occurred fifty-seven instances of proximal dilatation of the artery, a percentage of 12.7. Nine of the twenty-one cases studied in the Johns Hopkins Hospital showed proximal dilatation, a percentage of 43. It is obvious that observations in the 447 described cases are probably incomplete. William Hunter[3] in 1757, in giving us our first description of an arteriovenous aneurysm, noted proximal dilatation in the two cases recorded by him.

Broca[4] has described one of the most remarkable instances of proximal dilatation of the artery to be found in the literature:

The wall of this brachial artery is extremely thin, hardly one half millimeter in thickness; semitransparent, flabby and collapses like the wall of a vein . . . When flattened out, the vessel has a circumference of 80 mm. When the artery was distended by means of a cone (as it would have been if filled with blood) the circumference was 86 mm., much larger than the humerus. Below the arteriovenous communication, the artery suddenly narrowed and all at once resumed its normal caliber."

In a symposium on the subject of arteriovenous aneurysm at the Radcliffe Infirmary, Oxford, England, March 26, 1915, at which I was fortunate enough to be present, Sir William Osler[5] hesitated somewhat to attribute cardiovascular changes to the presence of the fistula:

"The changes in the arteries on the proximal side of the lesion are less striking, but sooner or later sclerosis occurs with dilatation, and sometimes with saccular aneurysm opposite the orifice of communication. Even within two months of the injury, the femoral artery may be felt to be larger and with stronger pulsation (Paignton case). Remote effects on the general circulation are rare, particularly in aneurysms of the head and arms. One of my patients (Case 3) died from heart disease which may have had some connection with his long-

* Reprinted from *Arch. Surg.*, 7: 64–82, 1923, with kind permission of the publishers. Eleven illustrations which originally appeared in the article have not been included.

standing lesion. In the leg, progressive dilatation of the vessels may lead to serious effects. In the case of Captain Mosher (reported in Lagarde's Gunshot Injuries, 1914, p. 281), wounded in the middle of Scarpa's space in 1898, at the time of death (1911) the dilated arteries extended from the bifurcation of the common iliac to the lower third of the thigh. Hypertrophy of the heart followed, and death from progressive failure of the circulation."

In the 447 recorded cases, cardiac dilatation and hypertrophy, of more or less marked degree, are noted in sixteen instances, accompanied occasionally by auricular fibrillation and myocardial decompensation. Six of our twenty-one cases showed enlargement of the heart, a percentage of about 28 as compared to a published percentage of 4. Two of Dr. Halsted's cases exhibited an enormous cardiac hypertrophy and dilatation, together with auricular fibrillation and evidences of chronic passive congestion, although previous to the formation of the fistula they had been entirely well.

Among the large number of interesting aneurysms treated at the Johns Hopkins clinic, the following case revealed certain phenomena which undoubtedly throw light upon the question of cardiac hypertrophy and proximal dilatation of the artery.

## REPORT OF CASE

*History.* C. W., a West Virginia miner, aged 41, was admitted to the Johns Hopkins Hospital, Aug. 9, 1922, complaining of vomiting, shortness of breath and weakness. He had been perfectly well until the age of 16, when he accidentally shot himself with a revolver carrying a 38 caliber bullet. The bullet entered the left thigh 4 inches above the knee, the knee being flexed at an angle of 45 degrees. Profuse bleeding from the wound of entrance followed the shot, the blood spurting 2 feet. A tourniquet was applied at once. Slight oozing continued until a physician removed the bullet, which was found lying beneath the skin on the anterolateral aspect of the leg, about 3 inches below the knee. A dressing was applied to the leg. There was a slight stain on the bandage after the removal of the tourniquet, but no further profuse bleeding. There was no noticeable swelling of the knee or of its under surface, and the patient could not recall any discoloration of the skin. He was able to stand on the leg immediately after the accident, but on the physician's advice remained in bed for a week and returned to work in the mine within ten days.

The patient apparently suffered no difficulty until five years previous to admission, when he was compelled to give up underground mining because he could not endure the bad air of the mines; he felt "knocked out" after only a short period of work. He began to be troubled with abdominal pains, which he attributed to the stomach. He was able, by changing to an open-air job, to do a full day's work during the next three years. For the last two years, he had done very little work, and none at all since January, 1922, when vomiting, extreme weakness, shortness of breath and smothering spells around the heart confined him to bed and kept him incapacitated until his admission to the hospital.

He could not remember the onset of the thrill which he himself felt around the knee. It had been present a long time, and he believed that it had appeared coincidentally with the swelling of the leg, which he noticed soon after the accident, apparently beginning just above the knee and extending gradually down the leg. This swelling appeared to be an actual increase in the size of the leg. The patient had noticed that his heart pounded rather forcibly, causing considerable distress in his head accompanied by a feeling of dizziness and faintness whenever he stooped over to raise things from the ground. He had also experienced marked discomfort in the epigastrium, which was accentuated with each beat of the heart.

*Examination.* The patient was a muscular, well developed man, with slight cyanosis of the face, but no respiratory distress. The pulse rate was 97; respiration, 24; blood pressure (left arm), systolic, 118, diastolic, 55. The erythrocytes numbered 3,844,000; leukocytes, 5,700. The hemoglobin was 70 per cent; Wassermann reaction, negative; urine, negative.

The first of many striking features was the extraordinary difference in size of the two limbs, the left thigh and lower leg being approximately half again as large as the right; another, the difference in the skin of the two legs, the right being perfectly normal in appearance throughout, the left thigh showing numerous small, dilated venules over the posterior and anterior surfaces, from Poupart's ligament down to the toe, these venules being

in the skin. In addition, there were numerous large, dilated veins in the subcutaneous tissue of the lower leg, and on close inspection it was evident that these veins were pulsating, an observation which was corroborated by palpation and by sphygmographic records. There was also a tan, spotted, freckled discoloration of the skin of the anterior surface of the lower leg and dorsal surface of the foot, such as one finds in varicose veins. The toes on the left showed a dark blue, purplish discoloration.

The third striking feature was the very forceful beating of the heart, which fairly shook the bed, lifted the cover, and caused a distinct movement of the entire thorax and abdomen with each beat. The visible pulsation over the precordial area was greatly increased, the region of relative cardiac dulness measuring 16.5 by 5 cm. The apex beat was in the fourth interspace, 15 cm. from the median line. There was a very forceful impulse at the apex, a well marked shock of the first sound, with a vibratory sensation following the shock. A soft systolic murmur accompanied the first sound all over the body of the heart. The extraordinary pulsation noted just below Poupart's ligament on the left was found, on palpation, to be due to a greatly dilated femoral artery, which measured approximately 2 cm. in diameter. The right femoral artery measured approximately 0.6 cm. in diameter. The dilated portion of this artery could be followed well down the thigh to a point where it entered the aneurysmal swelling in the popliteal space. About 2 inches below Poupart's ligament, there was noted, with each beat of the heart, a lifting of the skin along the course of a branch of the femoral artery, which was probably the lateral circumflex. The pulsation noted above the knee in the artery was visible below the knee in the greatly enlarged surface veins, which had formed small pulsating lakes of blood in the subcutaneous tissue. Above Poupart's ligament, there was a lifting of the abdominal wall with each heartbeat, and on palpation a large, strongly pulsating common iliac and abdominal aorta could be definitely made out. Liver dulness extended a finger's breadth below the costal margin on deep inspiration. The liver did not seem enlarged and no pulsation could be felt in it.

In the popliteal space there was a soft, pulsating, lemon-sized mass, which on palpation gave the characteristic thrill found in arteriovenous fistulas. This could be followed along the course of the artery into the abdomen, almost to the umbilicus, and downward as far as the ankle. With the stethoscope, a loud, whirring noise was heard, with systolic intensification. This bruit, which was heard best at the upper pole of the mass, extended along the vessels to the ankle and upward almost to the xiphisternum. There was no bruit over the liver area. The area of swelling in the popliteal space measured 6 cm. wide and 7 cm. in the vertical diameter. Pressure at the point of the greatest thrill, namely, at the superior pole of the swelling, resulted in complete obliteration of the continuous thrill, and presumably of the fistula.

This obliteration of the fistula was followed immediately by a remarkable reduction in pulse rate. Numerous observations were made, and a pulse which ranged around 88 before obliteration was reduced to 56 immediately on closure of the fistula. It was also noted that there was a definite increase in the force of the pulse immediately after obliteration of the fistula. This observation was confirmed by a series of blood pressure readings, which will be discussed later. Below the pulsating mass, an artery was felt leading down between the heads of the gastrocnemius muscle, considerably smaller in size than the artery which entered the mass at its upper apex. The posterior tibial pulse on the left was absent when the fistula was open, but on obliteration of the fistula a definite pulse was felt posterior to the internal malleolus. With the fistula open, there was a very slight pulse to be felt in the dorsalis pedis artery, which was markedly increased by obliteration of the fistula. There was a good posterior tibial and dorsalis pedis pulse on the right.

The reduction in pulse rate and increase in blood pressure were produced also by simply obliterating the left femoral pulse just below Poupart's ligament. An interesting feature was a recorded blood pressure in the right leg of 160 systolic, 86 diastolic; and in the left leg 220 systolic, 70 diastolic. The high systolic reading on the left was of necessity taken with obliteration of the left femoral pulse (with closure of the fistula), and the diastolic reading was obtained with the fistula open.

The surface temperature was remarkably increased on the left lower leg and foot as compared to the right, there being a recorded

difference of as much as 2 degrees (F.). The calf of the leg felt hot, and the patient stated that the left leg always felt warmer than the right.

The following special examinations were made: A teleroentgenogram, August 17, gave a combined measurement of 15.8 cm. An electrocardiogram revealed a normal mechanism. A second electrocardiogram was taken to illustrate the very significant changes in the pulse rate which occurred on obliteration of the fistula. Before closure, the cardiac rate averaged 72, with a P-R interval of 0.18. After closure of the fistula, the heart rate fell as low as 35, with a P-R interval of 0.20.

Numerous observations were then made to determine the variations in the general blood pressure on closing and on opening the fistula. Within five seconds after the fistula was closed by digital pressure, the general systolic blood pressure rose from a uniform level of 120 to 164, dropping within sixty seconds to a uniform level of 126. When the fistula was opened, the general blood pressure dropped 30 points, to 96, returning within twenty seconds to a level of 116.

The same phenomenon was noted with respect to diastolic pressure; an immediate rise from 66 to 90 was noted on closing the fistula, with a fall to a constant level of 84 within forty seconds. A drop to 48 was noted on opening the fistula, with a rapid return to the usual level of 66.

*Operation.* August 31, the patient was operated on by me, with the assistance of Dr. Mont R. Reid, formerly of the Johns Hopkins Hospital, and now at the Cincinnati General Hospital. The pulsating mass in the popliteal space proved to be a large sacculation of the vein just distal to the arteriovenous opening. Running distally from this sacculation was a vein greatly diminished in size, 0.8 cm. in diameter. The exposed portion of the vein proximal to the fistula was greatly dilated, with another sacculation above the first. Above these sacculations, the vein had a diameter of 1.8 cm. The artery was dilated, and its walls were markedly thinned, with a diameter, proximal to the fistula, of 1.8 cm., and a distal diameter of 0.8 cm. The fistulous opening led directly from the artery into the vein and had a diameter of 2.1 cm. as measured from the outside.

The operation was performed under a tourniquet. The artery and vein were separated, and the two slitlike lateral openings closed with fine silk, reestablishing the lumen of each vessel. The wound was closed with silk, and healed by first intention. Drainage in vascular surgery must be scrupulously avoided.

*Course.* Immediately after operation, a vigorously pulsating posterior tibial artery could be felt on the left, considerably stronger than on the right. Nine hours after operation, the patient said he felt much better than at any time previously, the distress of the vigorous pulsation in his head, which he had felt continuously before, having disappeared. Within five days, there was a marked change in the patient's general wellbeing. The precordial heave, which formerly shook the bed, had disappeared entirely, and he no longer complained of the constant throbbing in his abdomen and head.

Careful examination of the heart seven days after operation revealed no change in the relative cardiac dulness, but the large pulsating femoral artery, so strikingly visible in the left groin before operation, had greatly diminished. On palpating the femoral artery just below Poupart's ligament, one was struck by a remarkable decrease in its size; its approximate diameter appeared to be 1 cm., as contrasted with a preoperative diameter of 2 cm. September 12, thirteen days after operation, a teleroentgenogram recorded a heart shadow of a total width of 13.5 cm. as compared to a preoperative reading of 15.8 cm.

A gradual readjustment of blood pressure occurred. On the first day after operation, the systolic reading was 132, the diastolic, 105. The preoperative reading was: systolic, 120, diastolic, 66. This high reading gradually fell until the day of discharge, when it was: systolic, 104, diastolic, 73, the systolic reading being considerably lower than before operation, the diastolic somewhat increased. An apparent readjustment in the blood picture also followed the operation. Previous to operation the red cells totaled 3,880,000 per cubic centimeter. The second day after operation, the total was 5,500,000, indicating a concentration of blood. This high red cell count gradually fell until the day of discharge, when it was 4,480,000. The significance of this will be made clear later.

## COMMENT

The most startling feature in connection with the case was the behavior of the general

blood pressure dependent on conditions at the fistula. In looking through the hospital records, I could find very little information comparable to our present observations.

C. B., operated on by Dr. Halsted in 1916 for a fistula in the right Hunter's canal, had a very large heart with a hugely dilated proximal artery. Previous to operation, blood pressure readings ranged around 120 systolic, 60 diastolic (left brachial). No further comparable observations were made until six weeks after operation, when a blood pressure of 145 systolic, 114 diastolic in the left brachial artery was recorded; a rather remarkable increase, and apparently sustained over a long period of time.

Bramann[6] records a case of arteriovenous fistula of the ulnar vessels in which blood pressure readings were 58 to 69 systolic before operation, and 116 to 130 systolic after operation, as read by a Ludwig's manometer. In one of Dr. Reid's cases of arteriovenous fistula of the carotid and jugular vessels an unexplained bradycardia was present for several days after operation. Injury to the vagus at the time of operation was considered as a possible cause of this bradycardia, but it was most probably due to the altered condition in the general circulation following closure of the fistula.

### CAUSE OF BLOOD PRESSURE VARIATIONS

In seeking a cause for these blood pressure variations, I find that one can postulate what seems to be a well justified explanation on the basis of the physiology of the circulatory system. The same physiologic basis leads us to certain important and clarifying conclusions with reference to cardiac hypertrophy and proximal dilatation of the artery. Normally, the circulatory system, with reference to blood pressure, is a single closed system, namely, heart, arteries, capillary bed and veins, with a single pressure and a single peripheral resistance. The mean systemic pressure in such a system varies according to alteration in (1) total capacity of the system either by contraction or dilatation of the vessel walls; (2) total volume of circulating fluid; (3) heartbeat and cardiac output, or (4) peripheral resistance. An alteration in any one factor may call into action alterations in another, and the mean systemic pressure is dependent on a proper balance of these four factors.

Following the production of an arteriovenous fistula, there is an upset of this balance and a number of compensating changes are called into action. The original system (*a*), consisting of heart, arteries, capillary bed and veins, now gives place to two systems supplied from a common source, the second system (*b*) consisting of heart, artery, fistula and vein. The two systems may be pictured as two columns of blood with a common source of supply, but with a tremendous difference in peripheral resistance. It is an axiom that water will flow along the line of least resistance. Hence there would be a tendency for practically the entire blood volume to flow through system *b* if the difference in resistance to flow through the two systems is great enough. To maintain a flow through system *a*, therefore, it is absolutely essential to maintain a comparatively normal general pressure so that blood will flow through *a* as well as *b*.

### READJUSTMENTS FOLLOWING PRODUCTION OF FISTULA

Recalling the four factors concerned in maintaining a normal blood pressure, the readjustments which occur on production of a fistula may be enumerated as follows:

1. There is a great decrease in peripheral resistance, resulting in an immediate fall in blood pressure. Of course, blood pressure is not the result of peripheral resistance, but the general effect of the presence of such a peripheral resistance is to enable the heart to produce a high arterial pressure. Remove that resistance and blood pressure falls.

Efforts to compensate for this fall in pressure are several. Arterial pressure reduced to its simplest terms is the resultant of two factors: (1) the amount of blood entering the arterial system from the heart, and (2) the amount of blood leaving the arterial system through the capillaries, and in this case through the fistula. Therefore, to offset the greater volume of blood leaving the arterial system through the fistula, we must increase the amount of blood entering the arterial system from the heart.

2. Cardiac output, in turn, depends on several factors: (*a*) the amount of blood contained in the heart at the beginning of each contraction; (*b*) the strength with which the heart beats, and (*c*) the number of contractions per unit of time. The filling of the heart at the beginning of each beat is in turn dependent on the amount of blood which is available to

fill the cavities, and therefore on the pressure in the great veins. Increased frequency of heart rate alone need not necessarily increase the total output of the heart into the arterial system. If the veins are not filled more rapidly, it is not possible to obtain more blood to put into the arterial side, however frequent the heart beat. There will be, therefore, an optimum frequency of heartbeat which will depend on the state of filling of the great veins. The fuller these are, the more rapidly the heart may beat without diminution of total output.

In a fistula, there is a marked increase in venous pressure, a rapid filling of the great veins, and a probable dilatation also of the right side of the heart, which receives the increased blood from the overfilled veins. Bayliss[7] states that "the inflow from the veins is, practically, the determining factor in the work done by the heart." In a fistula, the inflow from the veins is greatly increased. This is due in part to the increase in velocity of flow around the system *b*. Velocity of flow varies directly as the difference in pressure between two points and inversely as the resistance between two points. In a fistula, there is a marked sudden difference in pressure between the two connecting points, the artery and vein, and a marked diminution in resistance, both factors favoring an increased velocity of flow from artery to vein, and therefore around the system *b*. If the work depends on the inflow from the veins, as Bayliss states, the work of the heart is greatly increased in an arteriovenous fistula, and the physiologic response to increased work is hypertrophy. The volume of blood which flows through the heart per unit of time is obviously greatly increased when a short circuiting of the flow occurs, as in a fistula. To take care of this increased volume of blood, the heart works more rapidly and with greater force, but, in the presence of a fistula, without a rise in blood pressure.

The great increase in cardiac effort was well illustrated in our clinical case in which the bed shook with each systole and in which operation brought relief from the excessive pounding of the heart. Following the operation, the blood pressure was maintained at a higher level in spite of a tremendous decrease in cardiac effort. The increase in pulse rate, and therefore in cardiac effort, is well shown in a number of experiments performed by me three years ago, under the direction of Dr. Mont Reid, in which fistulas were produced between the carotid and jugular vessels in a dog. The pulse rate was noted before and after opening the fistula, and at each operation there was an immediate rise in pulse to an almost uncountable rate: in Dog 1, from 140 to 220; in Dog 2, from 160 to 220; in Dog 3, from 150 to 180; in Dog 4, from 100 to 190; in Dog 5, from 110 to 192.

3. The third factor to be considered as taking part in the readjustment of arterial pressure in the presence of a fistula is the alteration in the volume of circulating fluid. Any lowering of blood pressure causes an absorption of fluid from the tissues into the blood. For example, the blood content during the last stages of bleeding may contain little more than from 50 to 60 per cent of the blood which was present in the first specimens, pointing to a corresponding dilution by tissue lymph. Our clinical case gives some slight evidence of this adjustment. A red cell count of 3,880,000 before operation is increased to 5,500,000 immediately after operation, pointing to a concentration of blood by loss of plasma when the larger volume was no longer needed owing to the repair of the fistula. This high red cell count dropped within two days to 4,800,000, indicating a gradual readjustment of blood volume. Experimental results are not available as yet, but blood volume studies are being made on our experimental animals by Dr. Harry P. Smith of the department of pathology. It is a point which should be demonstrable, as it is on the increase in total quantity of blood and primarily on the increase in volume of blood flowing through system *b*, that the dilatation of the artery depends. The sequence of events, which may again be explained on a physiologic basis, is probably as follows:

The fistula results in such a lowering of pressure in system *b* that the tendency is to divert a larger volume of blood through this route. To accommodate this increased volume of blood, there must be a widening of the blood stream, and particularly of the distensible elastic arterial wall and vein. With a fistula sufficiently large, it is obvious that practically the entire blood stream would be diverted through *b*, if it were not for the resistance to distensibility offered by the vessel walls. That the entire blood volume is not diverted through *b* depends, therefore, on the resistance offered by the fistulous opening and by the limited distensibility of the vessel walls. The volume

of blood through *b* will increase until the resistance to its flow through *b* equals the resistance to its flow through *a*. If the fistulous opening is small or if it is a mere slit, a point is soon reached at which the resistance at the fistula to the flow of the increased volume of blood equalizes the arterial resistance in *a*, thus establishing an equilibrium in the two systems. If the opening is large, the only resistance which can be developed is that offered by increasing the column of blood flowing through the opening, the size of this column of blood being limited only by the distensibility of the vessel wall; that is, the volume of blood flowing through *b* will need to be increased until the resistance offered by the fistula can be supplemented by the resistance to the flow of a larger volume through a tube of limited capacity. Hence, the dilatation of the vessel will depend in great measure on the cross section of the fistula—a narrow slit will afford considerably more resistance than a rounded opening, a small opening more than a large opening.

This increase in blood volume through system *b* is furnished from two sources: (1) an increase in total volume of circulating blood, (2) at the expense of blood flowing through *a*. That this increase in blood volume flowing through *b* is partly at the expense of blood flowing through *a* is suggested in our clinical case by (1) the dizziness and faintness of the patient on rising from a sitting posture, and (2) his inability to work in a mine, apparently owing to imperfect oxygenation of the tissues due to an inadequate flow of blood through them.

4. The last factor in the maintenance of pressure to be considered is the alteration in the total capacity of the system by contraction or dilatation of the vessel walls. Vasoconstriction occurs with fall in blood pressure, but contraction of the vessel walls in the presence of a fistula results only in a diversion of even more blood through system *b* and the fistula.

The extent to which these various factors are called into play in any fistula depends primarily on the size of the fistula and the resistance offered to the flow of blood through it. The fall in blood pressure depends wholly on the amount of blood which can be diverted through the fistula, and back to the heart. Similarly, any compensatory changes in cardiac output, in an increased blood volume and in alteration in capacity of the system will depend on the volume of blood diverted through the fistula, and hence on the size of the fistula. A small opening is easily taken care of, but a large opening suddenly acquired can conceivably result in immediate death; in fact, while we were working on the problem in 1919, as many dogs died on the table as lived following the opening of the fistula. These deaths were then unexplained, but they were probably due to too great a diversion of blood through the fistula.

The dilatation of the artery is then, I believe, dependent primarily on the cross section size of the fistulous opening; and dilatation will continue until the resistance at the fistula prevents any further increase in the quantity of blood passing through the fistula. I believe it can be proved experimentally that the artery will dilate over a period of years until the cross section of the artery equals the cross section of the fistula. In our clinical case, there was a history of gradual cardiac decompensation over a period of five years, and the reported cases emphasize the fact that the dilatation is dependent on the duration of the fistula.

### EXPERIMENTAL DATA

Our experimental evidence is still meager, but if our assumption that the entire process can be explained on physiologic grounds is correct, one should be able not once but always to reproduce our clinical picture in animals. Accordingly, a fistula was produced between the femoral vessels of a large mongrel (L 1), and numerous blood pressure readings were made by Dr. Alfred C. Kolls of the department of physiology, who collaborated with me in this experimental study. The tracings have been obtained by means of a modified Erlanger blood pressure apparatus which Dr. Kolls has adapted for use on a dog. Just previous to the release of the clamps used in producing the fistula, the following observations were made: pulse, 148; respirations, from 40 to 44; blood pressure, 204 systolic, 124 diastolic. The clamps were removed, and an immediate acceleration of pulse occurred from 140 to 224. Respirations were slightly increased, and the blood pressure had dropped from 204 systolic, 124 diastolic to 176 systolic, 80 diastolic.

On closing the fistula by digital pressure, the blood pressure readings revealed an immediate recovery to 208 systolic, 110 diastolic. A read-

ing with the fistula opened again was 200 systolic, 80 diastolic. Pressure readings below the fistula read 103 systolic, 30 diastolic, 135 systolic, 30 diastolic. November 3, readings showed a pressure of 190 systolic, 80 diastolic with the fistula open, and 205 systolic, 96 diastolic with the fistula closed. On the same day, a tracing showed the profound effect on systemic pressure produced by opening and closing the fistula. Digital pressure over the site of the fistula sufficient to obliterate the opening resulted in an immediate response, with an increased blood pressure and a diminished pulse rate. Readjustment occurred within a few seconds, and on opening the fistula, there was an immediate fall in pressure and an increase in pulse rate. Repeated identical observations were made, all illustrating the same variations in pulse and general blood pressure on the opening and closing of the fistula.

It is interesting to speculate on the reasons for the fall in pulse rate incident to closure of the fistula. Closure of the fistula results in a filling up of the aorta by the volume of blood which formerly leaked through into the veins. This produces an increase in aortic pressure which stimulates the depressor fibers of the vagus in the arch of the aorta, and reflex slowing of the heart is the result.

It is obvious from these records that very definite experimental evidence is available, confirming the clinical observations. Experiments are now under way to determine the effect of the size of the fistula on subsequent dilatation of the artery and on cardiac response. One can almost venture the prediction that dilatation will occur only if the fistula is larger in cross section than the cross section of the artery, and that the dilatation will then proceed until these cross sections are approximately equal.

## CONCLUSIONS

1. Proximal dilatation of the artery is explicable on purely physiologic grounds. It is dependent primarily on an increase in the total volume of circulating blood and more particularly on an increase of blood flowing through the system of heart, artery, fistula and vein, an increase in volume which is one of the compensatory changes necessary to rectify the fall in blood pressure incident to the greatly decreased peripheral resistance in the presence of a fistula.

2. Cardiac hypertrophy and dilatation are also explicable on purely physiologic grounds, hypertrophy being a response to the increased work necessary in handling the increase in volume of blood flowing through the heart per unit of time; and dilatation being the result of a general dilatation of the system, heart, artery, fistula and vein produced by the increased volume of blood flowing through it.

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# Some Problems of Peptic Ulcer

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IT is a pleasure and a compliment to be asked to contribute to a volume in honor of my old friend, Emile Holman. As surgeon, writer and man, and as one of the last of the Humanistic teachers in this era of the new mechanomedicine, he deserves our sincere tribute.

It is perhaps especially appropriate that I should summarize views on peptic ulcer which have developed during a medical lifetime, since Dr. Holman and I have broken many a lance through the years over these questions. As the Montagues and the Capulets were finally reconciled, I believe that our concepts have now come together, and happily, without a tragedy such as that of the "star-crossed lovers."

We do not propose to give a text book discussion of "peptic ulcer." That has been well done recently by others; in the monographs of Ivy et al.[1] and of Sandweiss[2] an innumerable array of what the *Autocrat of the Breakfast Table* calls "brute facts" are set forth. It is, however, necessary in introducing our argument to emphasize a few elementary concepts pertaining to the whole subject.

## GASTRIC AND DUODENAL ULCER ARE DIFFERENT DISEASES

Gastric and duodenal ulcer are often grouped together under the heading of peptic ulcer. However, it must be recalled that the classic descriptions of Cruveilhier[3] and of Rokitansky[4] dealt only with "round ulcer" of the stomach, and as recently as 1886 all that Fagge[5] had to say on duodenal ulcers was that they "not very infrequently arise after severe burns of the skin as Mr. Curling many years ago pointed out." Little more is heard of duodenal ulcer in the modern sense until Moynihan's[6] book in 1910.

There are several points in which gastric and duodenal ulcer seem to be fundamentally different. First, the two are not common in the same person; case after case of duodenal ulcer comes through without evidence over the years of gastric ulcer and vice versa. Second is the well known fact that what appears so often to be a simple ulcer of the stomach turns out to be cancer, whereas ulcer of the duodenum is always benign. Third, and very important, there is an entirely different pattern of gastric secretion in the two conditions. Careful measurements of basal gastric secretion showed that the findings with gastric ulcer were in pretty much the same range as normal controls, whereas with duodenal ulcer there was usually a profuse outpouring of thin, highly acid gastric juice.[7] (Fig. 1.) Finally, ulcer of the duodenum is often merely an incident in a chronic inflammatory disease which results in scarring and contraction of the entire area. Over the years ulcers form, heal and scar, and the mucosa breaks down again. Indeed with this distemper, aside from the hazards of bleeding and of perforation, it makes little difference whether at any time there happens to be an open ulcer. If the radiologist sees no crater, one nonetheless knows that there will be further breakdown in the future and evidence of repeated insults is usually found at operation or autopsy. This is all different from gastric ulcer.

## DIFFERENTIATION OF SYMPTOMS AND LESION IN DISCUSSION OF GASTRIC AND DUODENAL ULCER

Any intelligent discussion of the ulcer problem makes it necessary to consider symptoms and lesion as separate phases of the disorder. Only by so doing can one attempt to understand the mechanism and to plan treatment intelligently. *Symptoms and lesion do not necessarily go together.* Under the simplest measures symptoms often disappear and the patient feels perfectly well while the ulcer itself is unchanged. Conversely, symptoms may persist even after the lesion is ostensibly healed, as we shall explain hereafter. It is essential then in considering therapy to hold as necessary but separate objectives the relief of symptoms

and the healing (or elimination) of the lesion. It is very confusing to read about relapse rates after various methods of treating ulcer when the writer does not state whether the relapse is a recurrence merely of symptoms, of lesion or gastric acid;[8] others think that the ulcer itself is insensitive and that the disagreeable sensations associated with it are due to spasm or motor disturbance[9] usually in the pyloric region. It will perhaps simplify matters to

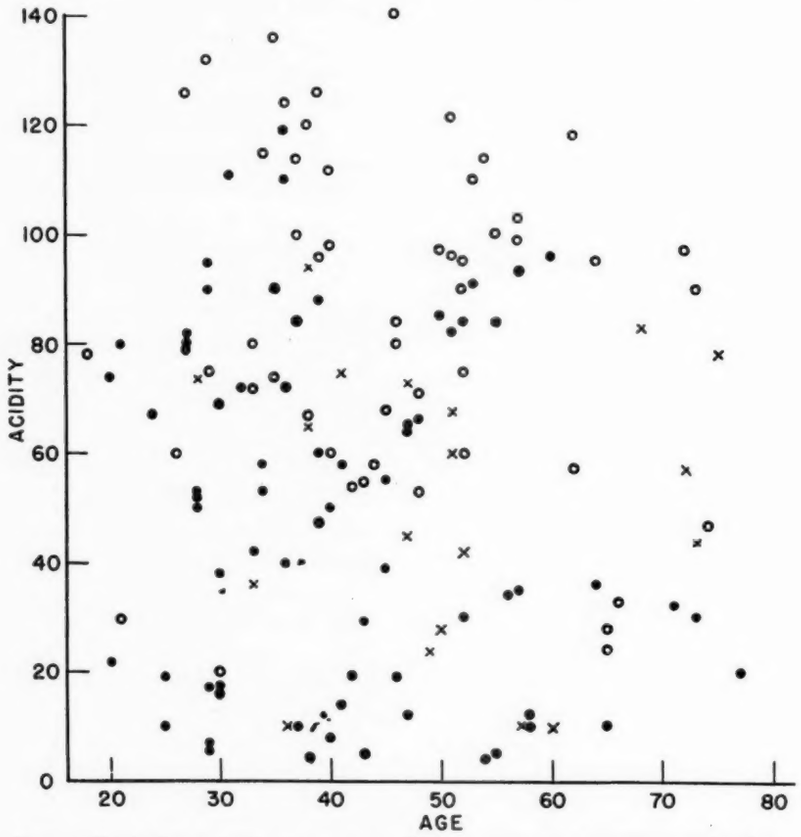


FIG. 1. Each dot represents one case: black, normals; crosses, gastric ulcer; circles, duodenal ulcer. (From BLOOMFIELD, A. L., CHEN, K. C. and FRENCH, L. R. *J. Clin. Investigation*, 19: 863, 1940.)

of both. The doctor has not done his job until both these objectives are attained.

### THE MECHANISM OF THE "INDIGESTION" SYMPTOMS OF GASTRIC AND DUODENAL ULCER

In uncomplicated ulcer the distress so often experienced after meals is compounded of elements of fulness, pressure, "gas" and burning. Like all fundamental sensations mediated through the autonomic nerves, this "pain" is often ill defined and not too sharply localized. As to its mechanism of production, few problems in clinical medicine have given rise to more bitter controversy. There are those on the one hand who believe the pain is always and only due to irritation of the lesion by present the arguments pro and con in tabular form. (Table 1.)

We have dealt with this subject at length elsewhere[10] and confess that we are strongly inclined to support the spasm theory rather than the acid irritation theory of mechanism of ulcer indigestion. This does not imply that acid may not play a part in producing the lesion. The recent work of Ruffin and associates[11] seems especially important. It occurred to them that one might study the effect of acid and of spasm at the same time. Patients drank a mixture of barium and acid and were then observed by fluoroscopy. The presence of the acid mixture in the ulcer crater did not cause pain unless obvious spasm was associated with it. They conclude: "From these observa-

tions the concept is advanced that abnormal motility is the fundamental mechanism through which ulcer pain is produced."

### ETIOLOGY OF PEPTIC ULCER

In this large field for speculation we shall touch on only a few points. First is the relation of ulcer to acid and peptic digestion of the gastric or duodenal mucosa. Acid may well play a part but it is surely not the whole story. Extremely high gastric acidity may exist without the appearance of any ulcer. (Fig. 2.)

TABLE 1
MECHANISM OF SYMPTOMS OF INDIGESTION

| *Evidence for Spasm* | *Answer* |
|---|---|
| An ulcer may perforate without any preceding pain | Center of ulcer is filled with granulation tissue without sensory nerves |
| Identical symptoms may occur in people with no ulcer | Ulcer is present but unrecognized |
| Symptoms may persist after excision | Another ulcer is present |
| "Indigestion" may occur in people without gastric acid | Mistake in measuring acid; it is not really absent |
| Relief of symptoms without change in acid | Rest has made pain mechanism insensitive and film of granulation tissue is already present |
| Reproduction by inflation of duodenum with a rubber balloon | Normal contractions are not painful. How can one get burning pain without acid? |
| Pain on contraction may be seen through gastroscope | |
| Ruffin's work with acid-barium mixtures (see text) | |
| *Evidence for Acid Irritation* | *Answer* |
| Relief of pain by alkali | Too little alkali for complete neutralization may be adequate for relief |
| | Relief often only after bringing up gas |
| | Relief by non-alkaline substances |
| Relief of pain by emptying acid from stomach | One does not remove the last film of acid covering ulcer |
| Reproduction of pain by reinjection of acid into stomach | Not constant—"pain mechanism" must be active |
| | Injection of acid may act by disturbing motility |
| Increase of gastric acid by steroids with activation of ulcer | Cortisone ulcers often asymptomatic even though acid is very high |

Second, gastric ulcer, much less often duodenal, may occur with normal or low values. (Fig. 1.) Next, the lesion, at least in the stomach, is local, usually with a site of predilection. If acid-peptic digestion is the whole cause why are not large areas of stomach digested away? Palmer and Buchanan,[12] following the older views of Virchow, have recently made a strong case in favor of "local ischemia" as a necessary precursor of gastric or duodenal ulcer. They point out the improbability of acid-pepsin alone being adequate to produce a chronic ulcer "without local depression of mucosal resistance" and they deplore the current overemphasis on secretory studies in this connection.

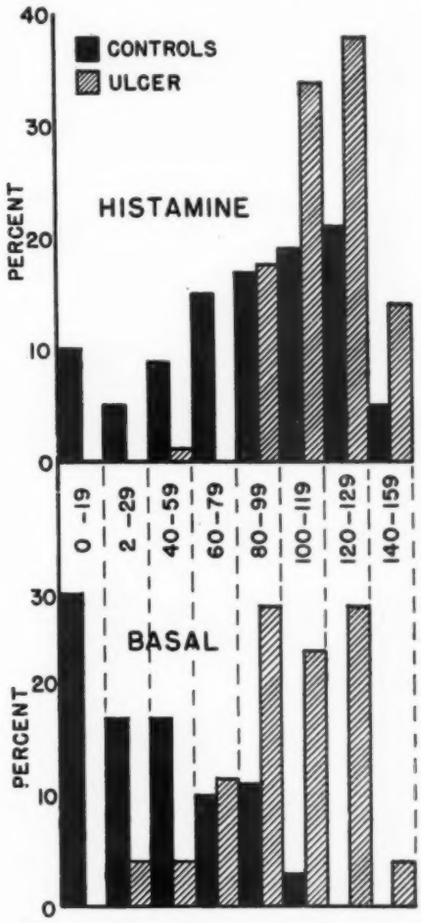


FIG. 2. Distribution curve of acidity (clinical units) in normals and duodenal ulcer with basal and histamine tests. (Modified from BLOOMFIELD, A. L., CHEN, K. C. and FRENCH, L. R. *J. Clin. Investigation*, 19: 863, 1940.)

At the present time what we may call the stress theory of peptic ulcer is much to the fore.

In all the older work on gastric fistula subjects (Beaumont,[13] Carlson[14] Wolff[16]) changes in the appearance of the mucosa and in the character of the secretions were observed under conditions of stress. Wolf and Wolff,[15] with their famous subject, "Tom," noted the

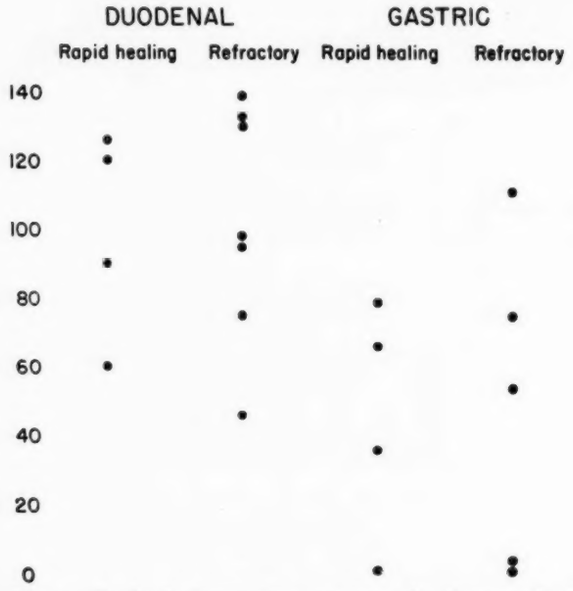


FIG. 3. Each dot represents one case showing speed of healing in relation to acidity. (From BLOOMFIELD, A. L. and FRENCH, L. R. *J. Clin. Investigation*, 17: 667, 1938.)

sequence of hyperemia, hypersecretion, hyperacidity, vigorous contractions of the stomach, washing away of mucus by thin abundant secretion and finally erosions which might go on to superficial ulcerations. However, inasmuch as ulcer may heal in a highly acid medium as we and others have shown[17] (Fig. 3), this cannot be the whole story either.

Our own views on etiology are summarized in Figure 4. The basic point seems to be that there must be a constitutional predisposition to ulcer. Unless this ill defined factor is present, no amount of stress or tension or indiscretion in eating seems adequate to cause ulcer, although the patient may develop other disorders such as hypertension. Granted the predisposition, then there are various factors which may precipitate a lesion or "indigestion" symptoms. In many people diet, for example, is obviously related to symptoms; it is much less clear that it is the direct cause of the lesion. The psychologic impact again may be paramount in causing symptoms and perhaps lesion, provided the predisposition is there. The speed with which sudden bleeding or perforation may come on under stress, as pointed out by Draper and Touraine,[18] is of great interest in connection with the recent views to be discussed hereafter.

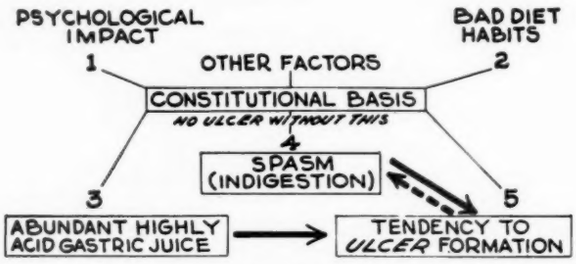


FIG. 4. Peptic ulcer. Treatment: (1) psychologic, environmental therapy; (2) eat slowly, chew well, ulcer diet; (3) alkali, atropin, vagotomy; (4) rest, antispasmodics, healing or excision of ulcer, plastic operation, vagotomy; (5) rest, sedatives, antispasmodics, control of high acid diet, surgery. (From BLOOMFIELD, A. L. *M. Clin. North America*, 8: 313, 1948.)

## NEWER THEORIES OF STRESS IN RELATION TO ULCER

Kirsner[19] has recently reviewed the information on hormones and peptic ulcer. It is quite evident, as shown by Gray and others,[20,21] that administration of ACTH or of cortisone may after a latent period of a week or so cause a tremendous increase of very highly acid gastric juice in certain people. The rapid production of gastric ulcer in some cases is now well documented. It becomes clear (Fig. 5) that what used to be thought of vaguely as an ill defined effect of stress or tension can be traced from psychic stimuli to hypothalamus to pituitary and finally to adrenal with outpouring of the effective steroids. There is also an overproduction of pepsin and uropepsin.

Of the vast number of people who receive steroids, only a very few develop ulcer. Many of these are known to have had ulcer in the past. All this supports our conviction that a constitutional "diathesis" must exist if any agency is to produce ulcer. So, too, butazolidin® and apresoline® seem to be occasionally effective in activating gastric ulcer. As to mechanism of symptoms, the outpouring of acid after cortisone is often unattended by ulcer "pain" even when ulcer forms—a point against the acid irritation cause of pain.

What is the relation of these phenomena to the production of gastric and duodenal ulcer? Is the increase in acid and pepsin directly

responsible or is this a by-product of some more subtle effective mechanism? All these questions are for future work and solution; as yet we do not know.

There is a tremendous field for further study here in which the real secret of the ulcer problem may lie hidden. It will be necessary to measure the gastric secretions of large numbers of people before and during cortisone administration and to correlate all this with symptoms, if any, and with the appearance (x-ray) of an ulcer. It is a monumental job but more worthy of support than some "projects" of which we know.

In summary, then, before there can be ulcer there must be a constitutional basis just as seems to be necessary if bronchial asthma or hypertension is to develop. Given this, a lesion may be precipitated by various factors, especially stress, through the pituitary-adrenal axis. Diet probably has more to do with causing indigestion than with the production of the lesion.

### COURSE AND PROGNOSIS

An individual ulcer may heal or may be excised; but since this disease is contingent on a constitutional tendency, a diathesis, which in our present state of knowledge cannot be eliminated, relapse or recurrence is always likely to occur. *The fundamental trouble is probably never cured.* The relapse may be one of lesion, of symptoms or both; the common finding of multiple scars of gastric ulcers at autopsy or of a chronically inflamed, scarred duodenum (chronic duodenitis) bears witness to this.

### THERAPY

*Objectives.* Some day a method or a medicine for eliminating the constitutional tendency may be found. At present there is no real cure, only palliation. Our objectives, therefore, are first the relief of symptoms and, equally important, the healing of the lesion. As long as ulcer remains there is a hazard of scarring, hemorrhage or perforation and, with stomach ulcer, the possibility that there may be cancer. As to the healing of any individual ulcer, it is to be recalled that there is great variation in the ease with which this can be brought about; there are easy and refractory cases. (Fig. 3.)

*Theories of Healing in Relation to Therapy.* The beneficial effect of rest, in the sense of relief from strain, becomes intelligible in terms of the stress theory described heretofore. Neutralization is emphasized by those who favor acid as the sole cause of ulcer; it is hard to disentangle its effects from other procedure simultaneously prescribed. In the relief of pain antispasmodics are paramount for those who believe that spasm activates indigestion symptoms. In open ulcer fasting is favored by those who think the stomach needs rest; this measure is opposed by those (Meulengracht[22]) who believe that food will neutralize a continuous highly acid secretion. Feeding is also favored by those who believe that improved general nutrition is helpful in the healing of ulcer. As one sees, in their straits "to do something" doctors have rallied their forces around one or another feeble standard and have rationalized with medical sophistry what they are trying to do. That patients improve, that ulcers heal are often difficult to prove to be the result solely of what has been prescribed; witness a few of the casuals once thought so effective and then dropped as useless by the method of common consent:* elimination of foci of infection; injections of amino acids (histidine); treatment with sex hormones; fever therapy; foreign protein therapy.

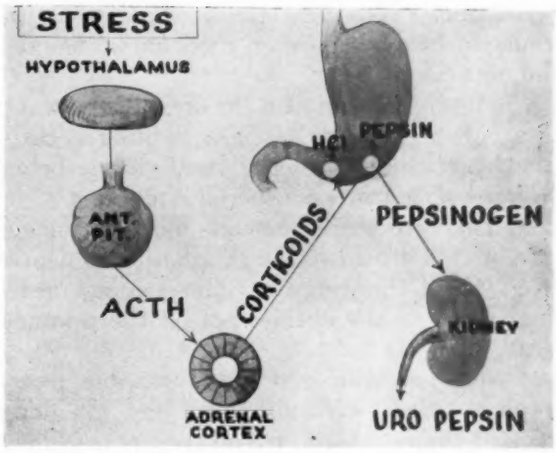


FIG. 5. The pituitary-adrenal axis in relation to gastric secretion (after Gray).

* "A more solid explanation is probably to be found in the development of a great body of unfavorable silent opinion. This silent opinion which kept in memory many failures, finally prevailed. Experience proves that, in the process of forming opinion as to the usefulness of a drug, those that are *for* speak out their minds, those that are *against* most often say nothing." (From HOUSTON, W. R. The Art of Treatment, p. 29. New York, 1936. Macmillan Co.)

Banthine,® for a time ascribed special virtue, seems to be just another good antispasmodic and antacid.

Vagotomy, recently on the crest of the wave as a cure-all in ulcer, is now fighting a rear-guard action to defend itself from being dropped except in very special situations.

At any rate there is clearly no total magic cure, no royal road to the elimination of peptic ulcer. All of the usual procedures (diet, medicine) work on the effects, not on the primary vice.

If what has been said in the previous paragraph is true, it obviously becomes ridiculous to split hairs about trivial points of diet, antacids, etc. It seems to be part of the tradition of gastroenterology that every up-and-coming specialist should have a diet and a "system" of his own. Thus, beginning with the great German "stomach men" of the late 19th century, we have "named" diets without number: the Leube, the Lenhartz, the Coleman, the Smithies, the Sippy, the Meulengracht, etc. If we search for the common factors in most of these, we find a simple bland diet eaten slowly and chewed well, served in small portions against a background of rest or relief from strain. Here faith, hope and the encouraging personality of the doctor also have a great chance to work. All this makes for conditions under which the stress factor tends to be lessened and the indigestion-promoting qualities of indiscriminate eating tend to be eliminated.

Of value then seem to be: (1) Rest, in the sense of relief from mental and physical strain. This may be achieved in or out of the hospital depending on the case. Enforced unwilling immobilization is of little value. Symptoms often go in a day or two; one must be sure later that the lesion is also healed. (2) Diet; how one eats is usually more important in chronic ulcer than what one eats. Often too little emphasis is placed on eating slowly, chewing well and not eating when under stress or in a hurry. Quick eating provokes the gastric feeding reflex[23] and may set up indigestion even in a person with a normal stomach.

We have no complicated named diet. Under a few days of fasting symptoms often clear up as if by magic. We follow this with a regimen of 100 cc. of half milk and half cream which the patient sips every two hours when awake (or some modification of this), and we finally go on to a simple plainly cooked diet from which are eliminated all coarse and tough foods, all very highly seasoned and spiced foods, and all very greasy foods. With patients intelligent and cooperative enough to grasp these simple principles a diet list is not often necessary.

Much has been said about antispasmodics. We still know of nothing better than tincture of belladonna given in adequate doses. Obviously a quantity too small to produce any effect will be useless. Supposedly "stronger" drugs such as banthine do not seem to accomplish more without disagreeable toxic symptoms, although some patients prefer them.

Finally comes the question of neutralization. In our hands good symptomatic results are achieved without attempting the almost impossible task of keeping the stomach alkaline at all times. Antacids are certainly useful if they relieve symptoms at the moment when they are distressing. Whether such relief is achieved by bicarbonate of soda or by some other alkaline agent seems to us of little consequence. Free use of alkalis may also lessen acidity enough to have some effect on healing of ulcer.

### SURGERY

While it is to be hoped that some day cure of peptic ulcer will be possible by a simple medicine, as of today we believe that chronic persistent or recurring ulcer is essentially a surgical disease to be treated usually by partial gastric resection. As regards gastric ulcer, the reasons are as follows: (1) the ulcer may be cancer; (2) the ulcer may become cancerous; (3) even if healed the ulcer scar may perforate; (4) even if apparently healed bleeding may still take place; (5) there is a great tendency to relapse. Regarding chronic duodenal ulcer: (1) it is essentially an incurable disease leading usually to (2) scarring duodenitis; (3) there is always the risk of relapse with bleeding or perforation, not to speak of pain.

I believe my colleague, Dr. Holman, agrees with this view. We have seen too many patients uncomfortable for ten or fifteen years on whom we regretted not having operated sooner.

From a clinical-physiologic standpoint the requisites of a satisfactory resection are:[24] (1) removal of the antral area in which hormones arise which stimulate acid secretion; (2) removal of much of the fundic acid cell-bearing area; (3) preservation of as much of the lesser

curvature as possible; (4) an appropriate stoma; in some quarters there is even a return to the Billroth I operation; (5) a short intestinal loop if Billroth II is used. By following these criteria we have usually had satisfactory results.

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# Evaluation of Results of Digital Flexor Tendon Grafts*

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A STUDY of the end results of flexor tendon grafting in the fingers and thumb reported in 1950[1] showed that when similar technic was used, the pathologic state of the tissues of the hand had a direct bearing upon the results, and likewise that a variation in technic improved the results in cases in which conditions were similar. In the fingers the results were measured as the distance by which the pulp of the finger failed to touch the distal crease of the palm—a single figure allowing direct comparison of results. In the thumb the angular deflection of the distal joint was used to measure the resulting function of the tendon graft. Assuming uniform conditions of the parts, it was found that the use of stainless steel wire as suture material and the use of the palmaris longus tendon as a free graft gave the best results. Kyle and Eyre-Brook[2] in a recent survey of tendon grafts indicate a preference for the sublimis tendon as a graft.

In this study we have utilized the findings of the previous report[1] and the additional consecutive cases of the last five years to bring the total number of grafts to 300. All cases were classified into one of four groups, based upon the preoperative findings. Those classified as "good" were ideal cases with good soft tissues, supple joints and without significant scarring. "Scar" designated a group where deep cicatrix from injury or previous operation left the tissues abnormal. Contractures were often present to a mild degree and in a few instances were severe enough to require preliminary plastic procedures before tendon grafting was done. The "joint" category comprised those in which there was limitation of passive motion, usually in the middle joint of the finger, which required mobilization by traction and active splinting before operation on the tendon. "Multiple" designated the group in which a graft was placed in more than one digit. Most of these could also have been classified as "scar" or "joint" cases.

The operative technic used throughout was basically the same, i.e., a full-length graft in the digit extending from the origin of the lumbrical muscle in the palm to the terminal phalanx. Bunnell's[3] method of suturing was used throughout, and in all cases a new insertion was made directly into the bone of the distal phalanx. Pulleys were reconstructed where necessary and by free graft if required, and in the last few years a separate non-absorbable suture was used to approximate the deep digital fascia at the mid-joint level, which here constitutes a minor pulley mechanism.

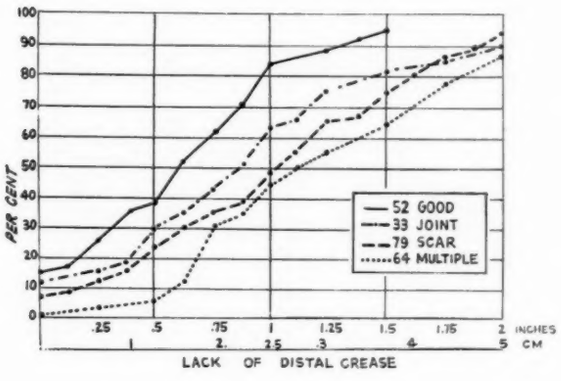
All measurements of function were recorded as the distance in inches by which the pulp of the finger failed to touch the distal crease of the palm, as well as the angular motion in each joint. In the thumb the arc of voluntary flexion was recorded as the numerator of a fraction, the denominator being the range of passive flexion. Conversion of this fraction into percentage thus gave a single figure. Results of a chosen group were then plotted on a chart which is cumulative in type. The resulting graph thus shows the total percentage of cases in the group which flex to any selected distance from the distal crease of the palm. If all cases were to flex completely, the graph would show a straight horizontal line at the 100 per cent level. By using this method of recording results, one can directly compare any two groups by noting which line more nearly approaches the theoretically perfect result.

Evaluation of any surgical procedure is difficult because the variables are many and it is usually not possible to state the results in an unequivocal figure. If we consider surgery, and especially surgery of the hand, as being a

* Read at the Meeting of the International Society of Orthopaedic Surgery and Traumatology, Berne, Switzerland, August 30, 1954.

specialized form of manual art, it should be possible to evaluate its results from the same standpoint as other arts such as sculpture, painting or simple cabinet making. The three elements common to all are a knowledge of materials, the application of proved principles and a specific technic. Considering these three as variables and using a single figure as a measure of the result, we can see the effect of each of these elements when the remaining factors are constant.

The charts presented herein show the results of various factors upon the final function of the digit and illustrate the effect of variation in one or more of these factors.

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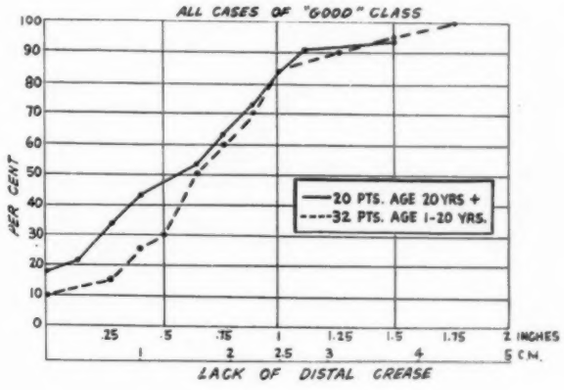


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FIG. 1. Shows the effect of the preoperative condition of the soft tissues upon the final results of a flexor tendon graft. The chart is cumulative in type, so that at any designated point on the horizontal axis the total number of cases flexing to that point is shown.

FIG. 2. Shows the effect of age of patient on end result. Age has relatively little effect upon the end results where the dividing line is twenty years. A further study of the results of grafts in the very young is not yet complete.

### EFFECT OF VARIATION IN MATERIALS

Using essentially the same technic and principles throughout, the results in the different groups of cases are shown in Figure 1. The presence of stiff joints, even though mobilized well before operation, lessens the final motion, and "scar" cases result in even more restriction. In this combined series the presence of damaged tendons and operative replacement by grafts in more than one digit has shown a less favorable result than in the 1950 report. The important point is that results are far superior in those digits without scar and with good joints. Thus primary treatment of injured tendons should be such as not to add to the scarring, and the joints should be kept supple if secondary operation is to have a fair chance.

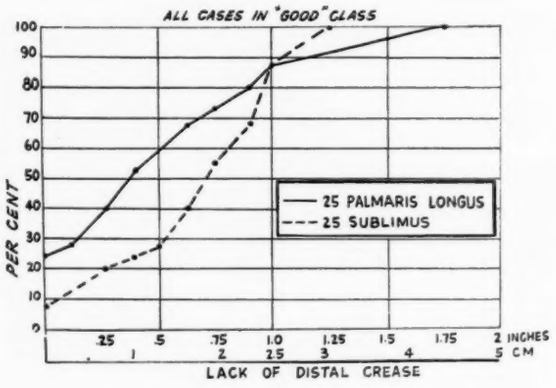
Age is commonly thought to be a factor. Figure 2 illustrates the results in twenty consecutive cases of two age groups. These were of the "good" class. The small difference in those that can flex to within ½ inch of the distal crease of the palm is probably not significant in such a small series.

### EFFECT OF VARIATION IN PRINCIPLE

The fundamental principle of a full-length tendon graft in the finger has not been varied, but the source and type of material used for the graft does alter the results. Figure 3 illustrates the difference in results in similar cases (all in the "good" classification) when comparing the use of the palmaris longus tendon to the sublimis tendon as a source of graft. The apparent poor showing of the palmaris is due to two cases: one a boy age eleven whose repair had been delayed five years, and the other a twenty year old man whose graft was made too long, as shown by the fact that when the proximal joint was held in extension the middle and distal joints flexed well. This should be counted as a technical failure. Both grafts were in the index finger, which in our experience shows less motion after flexor tendon grafting than does the other digits.

The palmaris longus tendon, when present, is almost ideal for a graft. It is usually of adequate length, small in caliber, and even when slipped out through two small incisions in the forearm has a thin, filmy layer closely adherent to the tendon. When the parts are scarred, there is perhaps more need for an extra paratenon layer so that in the "scar"

group a more deliberate block dissection is performed, either through one longitudinal or multiple transverse incisions. Figure 4 illustrates the results in "scar" cases, using three variations in source of the graft. The number of cases is small but there may be a definite essential to measure the results in all cases of a consecutive group before condemning one or the other method. Because of the small number, it would require but a few minor changes in results to reverse the upper two lines of the chart.

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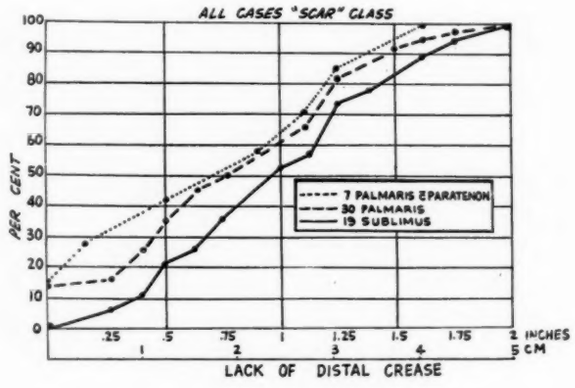


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FIG. 3. Shows the effect of graft source on end results. In "good" cases we believe there is little choice between the palmaris longus and the sublimis tendon as a graft, although preference is given to the former when available because of its more suitable size. In "scar" cases, however, its value is more marked. See Figure 4.

FIG. 4. Shows the effect of graft source on end results. Use of the palmaris in "scar" cases shows a definite superiority over the sublimis. The need for the extra paratenon layer is equivocal, since the difference here between the upper two lines is not significant.

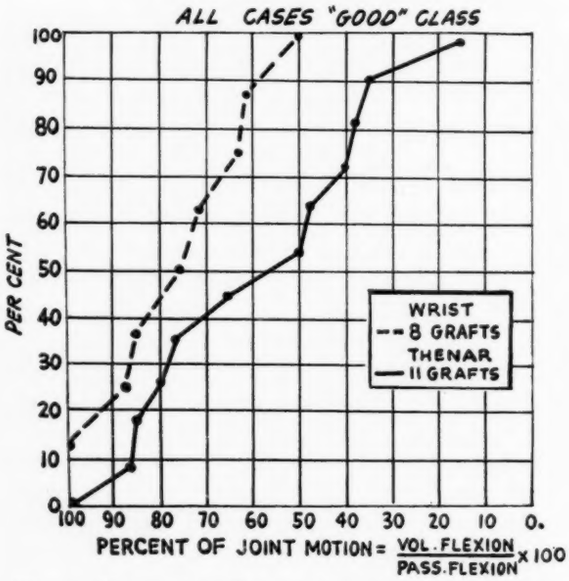



FIG. 5. Shows the effect of site of proximal suture. A graft in the flexor pollicis longus extending to the musculotendinous junction in the forearm is shown here to be of more value than one ending in the thenar eminence.

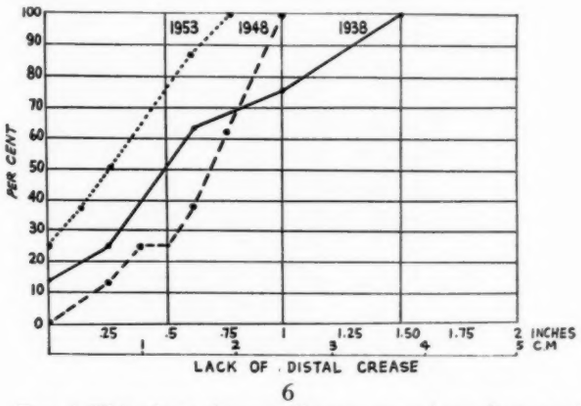
superiority in the extra paratenon layer. Unfortunately the impression of value of these variations is often based upon isolated cases without classifying as to type, so that it is

In flexor tendon grafts of the thumb we have an opportunity to see the effect of a direct change in principle. Eight grafts in which the proximal suture line was made at the wrist at the musculotendinous junction are compared with a group of eleven in which the proximal suture line was made in the palm in the thenar eminence. (Fig. 5.) The results are definitely better when the longer graft is used. However, there is one qualification: The late occurrence of lasting median neuritis in two instances when the graft was threaded through the carpal tunnel has caused us to use the short graft if the tendon is easily available in the thenar eminence. Obviously, if the proximal end has retracted, a longer graft is necessary.

### EFFECT OF VARIATION IN TECHNIC

In the previous report[1] improvement in results was seen when a change was made from silk to stainless steel wire as suture material. The use of a pullout wire also improved the results, as did the final plan of deliberate excision of all the remaining sheath except the pulleys. Figure 6 shows the results of eight flexor tendon grafts at three different periods. In 1938 silk was used for all suture lines. In

1948 wire was used combined with excision of the sheath, and the average result was better although no case had complete flexion to the distal crease of the palm. Eight consecutive cases treated in 1953 using wire and excising the sheath are shown with still better results.

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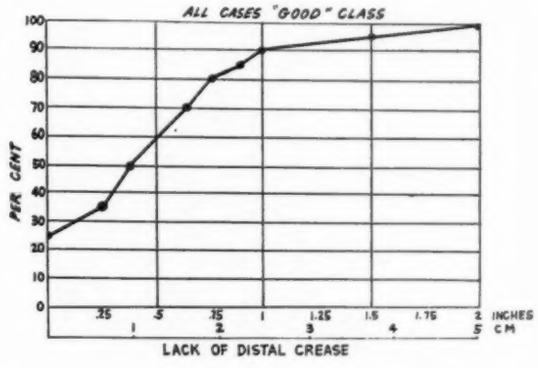


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FIG. 6. This chart shows a direct comparison of cases of similar status in which the only difference is in technic. In 1938 silk was used, and in 1948 wire combined with excision of the sheath. Between 1948 and 1953 the only essential change in technic, other than the added experience of the surgeon, was the deliberate resuture of the divided deep digital fascia in the finger which seemingly aids in better control of mid-joint flexion.

FIG. 7. The results in twenty consecutive "good" cases in which patients were operated upon in 1953 using the technic presently advised.

Since the number of cases is small, the results in twenty consecutive cases treated in 1953 are shown in Figure 7. These were all of "good" classification. The two cases which resulted in flexion to more than 1 inch of the distal crease of the palm are the same two shown in Figure 3 where technical error accounted for one, the graft being too long; the other was the result of a situation in which operation was performed five years after injury.

## CONCLUSION

The result of a surgical procedure can be evaluated in the same way the result of any manual art can be if three fundamentals—materials, principles and technic—are considered and if the result can be measured and recorded in a single unequivocal figure. In this study of flexor tendon grafts in digits a single figure represents the results and is easily visualized and recorded. This has enabled us to compare the results when variation in any of the three fundamentals is present.

Results of flexor tendon grafting in the digits are best when the tissues are least damaged, when a full-length graft is used and when exacting technic is followed. Under these conditions it has been shown that 25 per cent of all cases will result in flexion of the pulp of the finger to reach the distal crease of the palm; in 50 per cent flexion will occur to within ¼ inch and all will flex to within ¾ inch of the distal crease of the palm.

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# Massive Gastrointestinal Hemorrhage in the Presence of Portacaval Anastomosis

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THE part played by portal hypertension in the patient with cirrhosis of the liver and massive gastrointestinal hemorrhage is open to question. When this idea was popularized it was assumed that portal hypertension was the most important factor in causing the esophageal varix to rupture. Recently, with the development of the hepatic occluded pressure technic, there has been some evidence to suggest that although the successful portacaval anastomosis or hepatic artery ligation will lower the portal pressure immediately, this pressure eventually will rise again, presumably as collateral circulation develops.[9] It is possible, as Taylor and Egbert[2] suggest, that portal hypertension plays a much greater role in one case than in another, and that the secret of success, as with many other forms of surgery, will lie in the selection of the proper case for the operation.

We wish to report on a patient with known cirrhosis who had a successful portacaval anastomosis. In this case there was near fatal hemorrhage even though the pressure, as measured directly at the time of operation and later by the hepatic occluded method, was normal.

The fact that cirrhotic patients actually may bleed to death in the presence of large portacaval anastomoses has led such experienced clinicians as Snell[4] and Learmonth[5] to question whether the construction of an anastomosis between two veins of a mean diameter of 6 to 8 mm. actually could lower the portal pressure to any great extent. Beswick and Butler[3] reported an autopsied case in which a natural anastomosis occurred through a vein measuring 6.2 mm. internal diameter. There is no record of portal venous pressure in this case.

It is known also that severe hemorrhage from esophageal varices can occur without portal hypertension. Such cases have been reported by Mithoefer,[1] Friedman[6] and Nochimowski.[7] No extrahepatic obstruction was demonstrable in these cases. These authors believed that the varices in these cases were a congenital defect. This opinion is shared by Weinberg,[8] who reviewed 1,189 consecutive autopsies, finding 95 instances in which esophageal varices were demonstrated; in only 23 per cent was there associated liver disease. Furthermore, of thirty cases of Laennec's cirrhosis, varices were demonstrable in less than half. This figure would agree with our own experience. Taylor and Egbert likewise believe that many of the varices are congenital in origin.

## CASE REPORT

B. D. (No. E118017), an eight year old white girl, was referred to us for treatment of hematemesis and melena of twenty-four hours' duration.

The patient had been jaundiced at birth. This jaundice did not disappear but the child remained otherwise well until January, 1950, at which time hematemesis and melena started. In March, 1950, she was operated upon at a midwestern clinic where a diagnosis of cirrhosis of the liver and portal hypertension was made at operation. Splenectomy was performed. Following recovery from operation the patient continued to bleed intermittently. In April, 1951, at another midwestern clinic an end-to-side portacaval anastomosis was performed. In 1953 she had two episodes of tarry stools and hematemesis, which were treated supportively. One month before the present admission ascites appeared, which responded to salt restriction and mercurial diuretics.

Five days before entry a sore throat and cold developed associated with chills and fever. The patient was treated with penicillin therapy and seemed to be responding well. Twenty-four hours before entry she passed a large tarry stool and vomited 300 cc. of blood. A transfusion was started and the patient was sent to Stanford University Hospital.

Physical examination showed a drowsy, pale, slightly jaundiced child. Her pulse was 160 and

blood pressure 70/50. The abdomen was slightly distended and a questionable fluid wave was present. There was dark red blood in the rectum. After 750 cc. of blood were replaced, the patient's hemoglobin was 8.5 gm. with a red blood count of 2.42 million.

On two previous gastrointestinal examinations no esophageal varices had been noted, but on esophagoscopic examination gastric varices had been suggested.

At the present admission, the bleeding seemed to be slowing down as the child vomited only twice more. However, the stools, which were dark red at first, continued to be tarry. It was decided to explore the distal esophagus and stomach in the hope of finding the bleeding point.

On July 26, 1954, using a left thoracico-abdominal incision, the stomach was exposed. There were approximately 2,000 cc. of ascitic fluid in the peritoneal cavity. The liver was very small and nodular. It was noted that the abdominal and chest walls were almost avascular as compared to the extensive capillary and venous oozing usually noted in long-standing cirrhosis. No varices were noted on the outside of the stomach or esophagus. The fundus of the stomach was opened. On the lesser curvature just below the junction with the esophageal mucosa and overlying a gastric varix 6 mm. in diameter there was an old clot, from the center of which came a venous ooze. The area was transfixed by suture. A needle placed in a vein close to the hilum of the liver showed the venous pressure to be 20 cm. of saline.

The child recovered from the operation. As a check on the pressure measurement, the hepatic wedge pressure was measured and recorded as 19 cm. of saline.

The lack of chest wall collateral and properitoneal collateral as well as the pressure measurements were interpreted to mean that the portacaval anastomosis was patent. The patient was discharged on August 4, 1954, with no further bleeding.*

## COMMENTS

It is interesting to note that in this case there was none of the usual extensive abdominal wall and extraperitoneal oozing of blood so commonly seen in the cirrhotic patient due to the collateral circulation. This fact was interpreted to mean that the portacaval anastomosis was widely patent, and this was substantiated further by the low portal pressure as measured directly at operation. Had there been any induration or ulceration at the site of the bleeding, it might have been thought that we were dealing with a peptic ulcer which had no relationship to the cirrhosis. Peptic ulceration is known to be more frequent in cirrhotic patients than in the general population.

Of course it always is possible that there are hypertensive crises in the portal circulation as there are in the peripheral circulation, and that the esophageal leak may occur when the pressure is high. Dye et al.[10] have noted a variation of portal hypertension under medical management. In this clinic two patients have been followed up who in four measurements of hepatic occluded pressure have shown variations from 18 to 39 cm. of saline with no change in their respective clinical pictures.

It is suggested, therefore, that the evidence presented by this case is further support for the suggestion that it is not necessary for a cirrhotic patient to have portal hypertension to bleed massively, and therefore the part played by portal hypertension is a variable one.

* Since this report was written, this patient died on December 22, 1954, in hepatic coma without further hemorrhage.

## SUMMARY

1. A case is reported of severe gastrointestinal hemorrhage in a known cirrhotic patient with a successful portacaval anastomosis in whom the pressure was measured within the normal range directly at operation and later by the hepatic occluded method.

2. Massive gastrointestinal hemorrhage can occur in the cirrhotic patient without portal hypertension.

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# Hypertrophic Pyloric Stenosis in the Adult

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HYPERTROPHIC pyloric stenosis in the infant is a medical entity whose diagnosis and treatment are well known now to almost every medical student. However, the same disease is a rarity in the adult and it is practically unheard of to make such a diagnosis preoperatively beyond infancy. We recently encountered the following case:

## CASE REPORT

M. C., (SUH 329503) a thirty-seven year old, white male tree surgeon entered Stanford University Hospitals on November 2, 1953, with a chief complaint of nausea, vomiting and abdominal pain of six months' duration. Two years before admission he had had the gradual onset of postprandial vomiting accompanied by some epigastric pain and tarry stools. He improved on an ulcer diet. Four or five months before this entry he was again bothered by postprandial pain, nausea and vomiting; the pain was relieved best by lying down. Gastrointestinal x-ray series were interpreted as showing no ulcer six months previously at a country hospital. Vomiting now followed the intake of almost any food. There had been a 16 pound weight loss in six months. Physical examination revealed a thin, middle-aged man in moderate abdominal distress. Temperature was 37°C., pulse 76, respirations 16 and blood pressure 100/65. The findings were not remarkable otherwise except for the abdomen where there was marked epigastric tenderness. No organs or masses were palpable. There was active peristalsis. Laboratory data revealed the following: white blood count 7,000, hematocrit 47. Gastric analysis: total acid 24 degrees, free acid 12 degrees. Gastrointestinal series revealed an organic, constricting lesion of the pylorus and prepylorus with ulceration, probably carcinoma. (Figs. 1 and 2.) Exploratory operation was done November 4, 1953. A firm whitish mass involving the pylorus was found and assumed to be carcinoma, localized to the pylorus. On this basis subtotal gastric resection was carried out using a closed aseptic technic. Twelve hours following surgery, because of

FIG. 1. Barium meal showing fixed deformity of pylorus.

evidence of hemorrhage, the abdomen was reexplored and bleeding was found in the aseptically closed greater curvature. Hemostasis was secured and the greater curvature of the stomach was closed in an open fashion with a locking stitch. The patient's postoperative convalescence was uneventful following this and he was discharged home ten days after surgery. One year following surgery he had gained 24 pounds and was asymptomatic.

Pathologic report of the resected specimen revealed the following: Grossly a firm, white mass occupied the pyloric canal, bulging into the gastric antrum. There was no evidence of ulceration in the stomach or pylorus. Photomicrograph (Fig. 3) shows marked thickening of circular muscle in the pylorus. No evidence of

FIG. 2. Spot films of barium meal showing fixed deformity of pylorus.

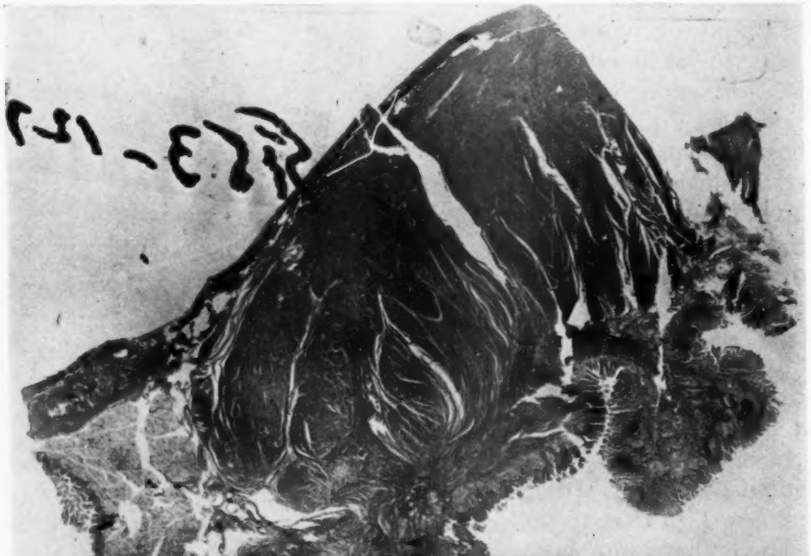

FIG. 3. Photomicrograph of the markedly thickened pyloric musculature.

ulceration or tumor in the stomach or pylorus was found. The pyloric mucosa showed infiltration by lymphocytes and plasma cells. Diagnosis was hypertrophic pyloric stenosis.

The pathologic report was indeed surprising, both because we were not familiar with the disease in the adult and because a much simpler and less formidable procedure than gastric resection might have been curative. This was the stimulus to investigate how hypertrophic pyloric stenosis in the adult could be diagnosed before surgery and just what the ideal treatment should be.

## FINDINGS

A review of the literature reveals that in 1835 Cruveilhier described a condition which

he termed adult pyloric hypertrophy and thought to be an inflammatory condition involving only the pylorus with hypertrophic features superimposed on certain layers of the muscle.

In 1885 Maier[15] published a description of thirty-one autopsied adults with pyloric hypertrophy which he considered to have been present in mild form from infancy.

In 1890 Billroth stressed a similar condition of the pylorus and termed it idiopathic, benign, hypertrophic pyloritis. Some writers term this Billroth hypertrophy.

In 1933 Kirklin[14] reported eighty-one cases of adult hypertrophic pyloric stenosis from the Mayo Clinic. Only one of these was correctly diagnosed before surgery. However, a small number of cases has been reported in which the correct diagnosis was made before or at surgery and treated by a Ramstedt procedure, pyloroplasty or gastroenterostomy. These are as follows:

Graham[9] reported an adult case cured by a Ramstedt procedure in 1920.

In 1925 Bastianelli[2] reported four successful Ramstedt procedures in adult hypertrophic pyloric stenosis.

In 1928 Crohn[6] reported a case in which gastroenterostomy was employed to treat an adult suffering from hypertrophic pyloric stenosis.

In 1930 Morton[19] reported three cases which were diagnosed before or at surgery and treated, one by a Ramstedt procedure and two by pyloroplasty.

In 1932 Stone and Ruggles[21] reported two cases successfully treated by a Fredet-Ramstedt operation.

In 1933 Judd and Thompson[12] reported four cases treated by a Fredet-Ramstedt procedure, but they do not mention the follow-up results.

In 1944 Wakefield[22] reported a case of pyloric obstruction which was followed for two years and finally treated by local resection of the pyloric muscle tumor.

In 1949 McCann and Dean[16] reported a case which was diagnosed at surgery, treated by pyloroplasty, and later required gastroenterostomy.

*Pathology.* All authorities agree that the essential pathologic feature is hypertrophy of the pyloric musculature, particularly the circular muscle. The hypertrophy, which may be so great as to occlude the lumen of the pylorus almost completely, forms the tumor that is characteristic of the disease. However, there is much disagreement and lack of knowledge about the etiology of the disease.

*Etiology.* Since formerly many advocated medical rather than surgical therapy, it is reasonable to suppose that some infants survived and grew to adulthood with the abnormality. Some of the reported adult cases gave a history of stomach trouble since childhood; more specifically, intermittent vomiting and signs of partial obstruction to the outflow from the stomach. Perhaps the stenosis in infancy was not marked, thus escaping clinical detection, and only in later life did complicating pathologic conditions in the stomach or duodenum accentuate the abnormality and bring it to a clinical level. In favor of this explanation are the statistics that the disease in both infants and adults occurs 80 per cent of the time in males. However, other patients with this affliction are completely symptom-free until early middle life when they develop the typical pain of peptic ulcer, relieved by antacids, with signs of pyloric obstruction, not relieved by medical management. At operation such patients show a gross pathologic disorder only in the pylorus, which on microscopic study reveals hypertrophic pyloric stenosis. Our case fell into this category. However, microscopic examination of the stomach and duodenum, although not demonstrating a true ulcer, usually does show evidence of gastritis or chronic inflammation of the duodenum which is not seen in patients without pain but with low grade obstructive symptoms from birth. In the situation in which symptoms first arise in adulthood, one can easily reason that spasm may cause the hypertrophy and that the spasm is usually secondary to associated disease such as peptic ulcer, gastritis or cholecystic disease.

Of the eighty-one cases reported from the Mayo Clinic, fifty had associated peptic ulcer, cholecystic disease or chronic appendicitis. On the other hand, a diagnosis of spasm is often made but never pyloric stenosis. Are the diagnoses of spasm perhaps incorrect, or could they have subclinical degrees of stenosis? Perhaps only certain pyloric muscles become hypertrophic under the influence of spasm through anatomic or autonomic dysfunctions

unknown to us. Others believe that only long-continued spasm can cause marked hypertrophy of pyloric musculature. Microscopic study, however, did not show any lack of ganglion cells in our hypertrophic pylorus which is evidence against this disease being similar in origin with Hirschsprung's disease.

Some authors have ruled out spasm or reflex spasm stating that these would cause real compensatory work hypertrophy of the muscle, which in their opinion is not the case, and that also an ulcer or ulcer-like history would be expected. However, a check shows that an ulcer-like history of pain is present in at least 50 per cent of the reported cases.

We should not forget that whether we decide the hypertrophy began in childhood or in adulthood, we do not know the cause of the original hypertrophy unless we accept the explanation previously set forth.

The explanation of the actual hypertrophy of the muscle, irrespective of its time of development, besides including spasm or reflex spasm even in the neonatal period, includes hyperadrenalism. Those favoring this view state that stimulation of pancreatic secretion is inhibited by excessive adrenaline and that lack of pancreatic secretion acts to delay the neutralization of the acid chyme from the stomach, thereby causing the pylorus to remain closed for a long time. In this manner it is suggested that gastric retention produces gastric hyperacidity with subsequent pylorospasm and pyloric hypertrophy.

In summary, we can say that there seem to be two varieties of hypertrophic pyloric stenosis in the adult. There is one in which the symptoms have been present in varying degrees since childhood, without pain, only to have the obstruction accentuated in adult life. These seem to be persistent infantile cases. We have no good explanation of how the hypertrophy originated in utero or during infancy. The other general category is the hypertrophy that gives symptoms only in adult life, usually those of peptic ulcer disease or less commonly of cholecystic disease; at operation only pyloric pathologic disease is found, the gross peptic disease probably being temporarily quiescent. These cases may well be explained by long-standing spasm of the pyloric muscle secondary to a reflex mechanism initiated by peptic ulceration, cholecystic disease or chronic appendicitis.

## TREATMENT

Once the diagnosis of intractable, pyloric obstruction is made, exploratory operation is clearly mandatory, as there are no criteria to differentiate benign hypertrophic pyloric stenosis from carcinoma of the antrum or pylorus, leiomyosarcoma or lymphosarcoma of the stomach. A number of radiologists have listed certain criteria which may point toward a diagnosis of hypertrophic pyloric stenosis. Kirklin has emphasized the striking concavity of the base of the duodenal cap caused by the pressure of the markedly thickened pylorus. Other radiologic criteria, as listed by McNamee,[18] are a concentric and elongated pyloric canal, widening of the pyloric sulcus and a constant, unchanging appearance of the pylorus.

Archer states that if there is a persistent, practically unchanging increase in the breadth of the pyloric ring on repeated examination, not amenable to antispasmodics, and a six-hour residue, the diagnosis is practically as positive as is the usual diagnosis of ulcer or carcinoma. Although ulcer and carcinoma should be kept in mind, the suspicion of benign hypertrophic pyloric stenosis before surgery may alert the surgeon to the recognition of this lesion at the operating table.

Once the surgeon is cognizant of this lesion, how can he recognize it grossly on abdominal exploration? Undoubtedly, a great many cases will be indistinguishable from the malignant lesions in this area. On the other hand, there are reports of cases in which the lesion was exactly that seen in infancy—a firm, white, glistening, circumscribed, soft and yielding mass without any other abnormalities.

Our case was similar to this, but we did not recognize it because we were not familiar with the occurrence of hypertrophic pyloric stenosis in the adult.

In those cases in which there is stenosis associated with gastric or duodenal ulceration or in cases in which there is question of malignancy, a gastric resection is, of course, indicated. However, when the disorder is localized and typical of that seen in infancy, a more conservative approach might be justified, or even sought. Among such approaches we might include pyloroplasty, local resection of the pylorus with a Billroth II type of re-establishment of continuity, gastroenterostomy and

last, but not least, the classical Fredet-Ramstedt pyloromyotomy.

It would seem that if the disease was localized, pylorectomy would be safe even if it was cancer, since the pylorus could be opened after removal, and if necessary, a frozen section made. Gastroenterostomy has the disadvantages that one does a less physiologic procedure than pyloromyotomy and may overlook a malignancy. If the lesion was classic for hypertrophic pyloric stenosis, the Fredet-Ramstedt operation should be performed as it is much simpler and safer than a resection.

A few such operations have been successfully performed in adults with this condition, and it seems reasonable to expect a wider application of pyloromyotomy if more surgeons become aware of the existence of hypertrophic pyloric stenosis in the adult.

SUMMARY

1. A case of adult hypertrophic pyloric stenosis is presented which was unsuspected at operation and treated as a malignancy of the pylorus.

2. The etiology, pathology, clinical recognition and treatment of adult hypertrophic pyloric stenosis is discussed.

3. It is suggested that the knowledge of the existence of this disease in adults may result in a more conservative surgical approach to its correction in selected classical cases.

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# Prepubertal Malignant Melanomas

## REPORT OF TWO CASES

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WHILE reviewing 101 cases of malignant melanoma in 1953,[1] Dr. Walsh and I found one of a four year old boy who had malignant melanoma with metastases to regional lymph nodes. Shortly after reporting these cases we had a second patient, a two year old Negro girl in whom malignant melanoma developed in a congenital giant hairy nevus. The tumor recurred, metastasized very widely and resulted in death seven months after the first nodule was noted. Our experience with two cases of malignant melanoma in children in a comparatively small series of cases was at variance with previous reports, and it has prompted us to review the recent literature on the subject and to report these two cases.

### CASE REPORTS

CASE 1. W. S., a four year old white boy was seen in the Stanford Children's Clinic on April 10, 1945. He had had a "bleeding wart" on the tip of his right elbow for several weeks. There was no history of a pre-existing mole or wart. Examination showed a rough, raised, pink area, measuring 1 cm., on the back of the right elbow. The lesion bled on slight trauma. In the right axilla there was a hard lymph node measuring 1 cm.

The first clinical diagnosis was "pyogenic granuloma." Five hundred roentgen units were given and this produced complete epithelialization, but the nodule persisted. The nodule was then excised under local anesthesia in the Surgical Outpatient Department. (Figs. 1 and 2.) The pathologic report of May 24, 1945, was as follows: "Section shows the surface epithelium raised and the papillae of the corium widened by a tumor which extends into the subcutaneous tissue and down to the basal line of resection. The tumor is cellular and is composed largely of large polyhedral cells, but there are also many spindle-shaped cells. These cells have a vesicular nucleus with a prominent nucleolus. Mitotic figures are present, but not very common. The cytoplasm is indisinct, pale and basophilic. The cells form acinar clusters with little intervening stroma. No pigment intra or extracellular is found. Two clusters of tumor cells are seen within endothelial lined channels. There is moderate polymorphonuclear leucocytic and lymphocytic infiltration of the stroma. This is an amelanotic melano-carcinoma. The diagnosis is: Melanoma, malignant, skin, elbow, non-pigmented."

On June 9, 1945, the primary lesion was more widely excised and the right axilla dissected. No tumor was found in the tissue excised from the elbow. Eighteen lymph nodes were sectioned and two contained tumor similar to the original skin specimen. (Fig. 3.) The diagnosis was: "Melanoma, metastatic, axillary, lymph node, multiple."

There was no evidence of recurrence or metastasis until October 10, 1946, when a small nodule was noted in the scar on the elbow. On January 30, 1947, the nodule was excised and was found to contain tumor identical to that of the primary and the axillary metastases. (Fig. 4.) Again tumor cells appeared to lie within endothelial-lined spaces. The diagnosis was: "Melanoma, malignant, skin, elbow, non-pigmented, recurrent."

Follow-up examinations have shown no recurrence or metastases. The last examination was on August 26, 1954. (Fig. 5.) A minifilm of the chest on that date was also negative.

*Comment.* This four year old boy had an ulcerated, repeatedly traumatized, non-pigmented malignant melanoma on his elbow. Two axillary lymph nodes contained metastases. Eighteen months later a local recurrence was excised. There is no evidence of recurrence or metastases nine years after the first operation

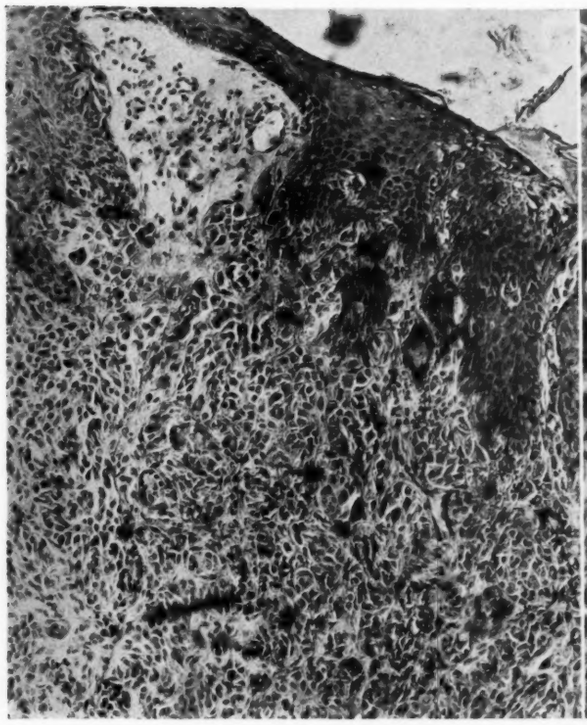

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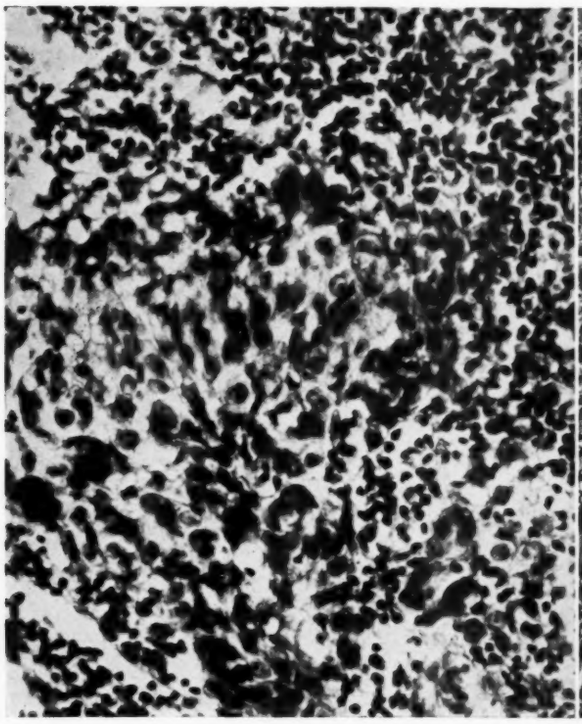
FIG. 1. Case 1. Primary malignant melanoma excised from the elbow.

FIG. 2. Same case. High power view from the primary malignant melanoma.



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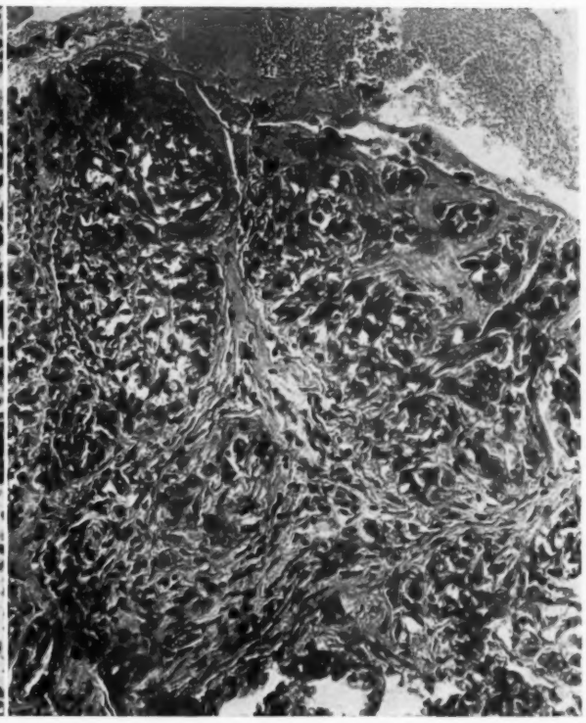

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FIG. 3. Same case. Metastatic melanoma in the peripheral sinus of an axillary lymph node.

FIG. 4. Same case. Recurrent malignant melanoma in the scar on the elbow eighteen months after the original excision.

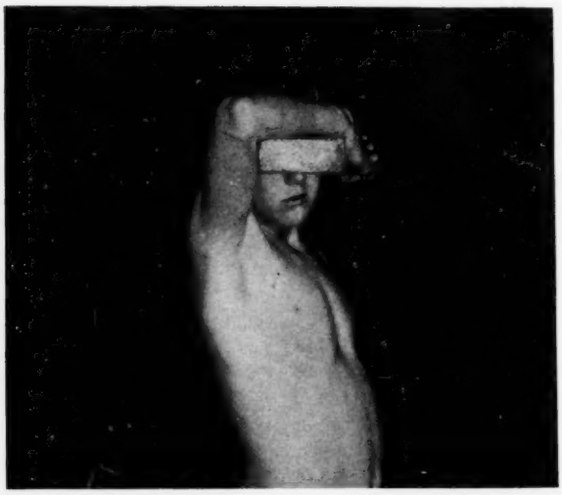


FIG. 5. Same case. Patient now thirteen years old. Scars on right elbow and in right axilla.

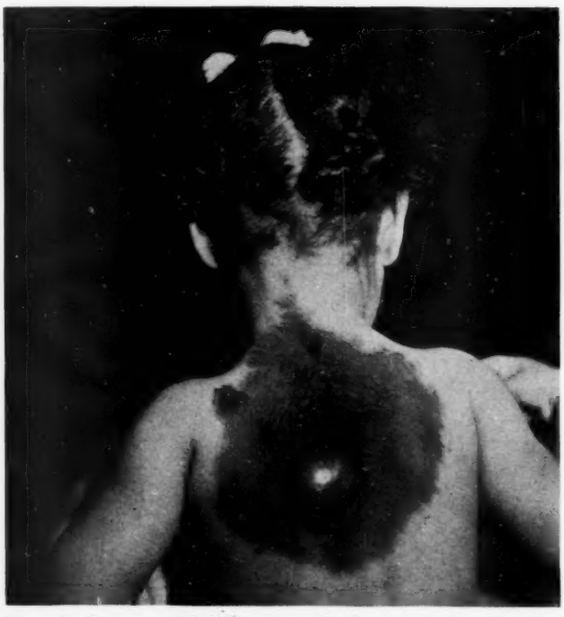


FIG. 6. Case II. Malignant melanoma growing in the giant hairy nevus.

and seven and a half years after the excision of a local recurrence.

CASE II. J. H., a two year old Negro girl, was born with a large hairy nevus on her back. When she was eighteen months old a nodule appeared in the lower central part of the nevus. (Figs. 6 to 8.) This nodule grew and measured 4 cm. at the time it was excised on January 13, 1953. The pathologic report was as follows: "The epidermis over the tumor is thinned and the basal layer is flat and heavily pigmented. A band of fibrous tissue containing clumps of melanophores separates the epidermis from the tumor and there is only equivocal junctional activity in the epidermis overlying the tumor. The tumor itself is made up of large masses of similar cells which have round or oval dark staining nuclei which vary in size and are generally rather large. No nucleoli are visible. Mitoses are easily found. There is only a narrow rim or no cytoplasm at all seen on the tumor cells. Some pigment is produced within the tumor and in some areas tumor cells appear to be present in vascular spaces. There is only a very scanty stroma so that many fields of apparently free nuclei are seen. The diagnosis is: Melanoma, skin, back, juvenile type. Nevus, back, compound."

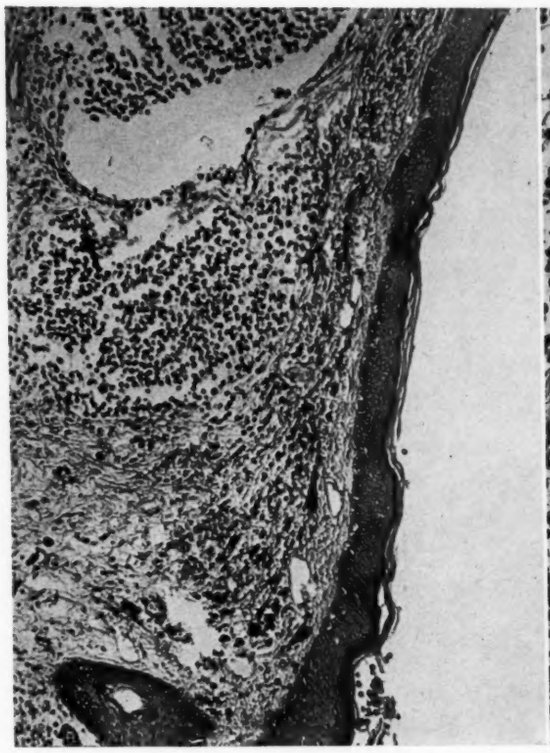
There was a prompt recurrence of the tumor. On March 10, 1953, three nodules were noted growing beneath the large nevus and there was a mass of nodes in the left axilla. (Figs. 9 and 10.) It was soon apparent that the previously quoted pathologic report was incorrect. This was a malignant melanoma and not juvenile melanoma.

On April 4, 1953, triethylene-phosphoramide (TEPA) was started, injecting 1.5 mg. daily for ten days. Three times a week 1.5 mg. was than injected until April 23, 1953. A maintenance dosage of .2 mg. was then injected three times weekly for four more weeks. As far as could be determined the two months of therapy with TEPA produced no beneficial effects. All of the masses continued to grow rapidly.

The patient was admitted to the San Francisco Hospital on June 8, 1953. There was a huge mass, measuring 17 by 37 cm., filling the left axilla, abducting the arm and extending from the right posterior axillary line around the left chest to the left side of the sternum. X-ray examination showed metastases to the left femur.

The blood on June 8th showed the following: hemoglobin 12 gm, packed cell volume 37 per cent, 7,000 leukocytes with 59 per cent polymorphonuclears and 39 per cent lymphocytes. The urine was negative.

The administration of aminopterin, .5 mg. twice daily, was started on June 13, 1953, but was discontinued on June 20th because of noesebleeds and the continued extremely rapid growth of the tumor. The patient died on



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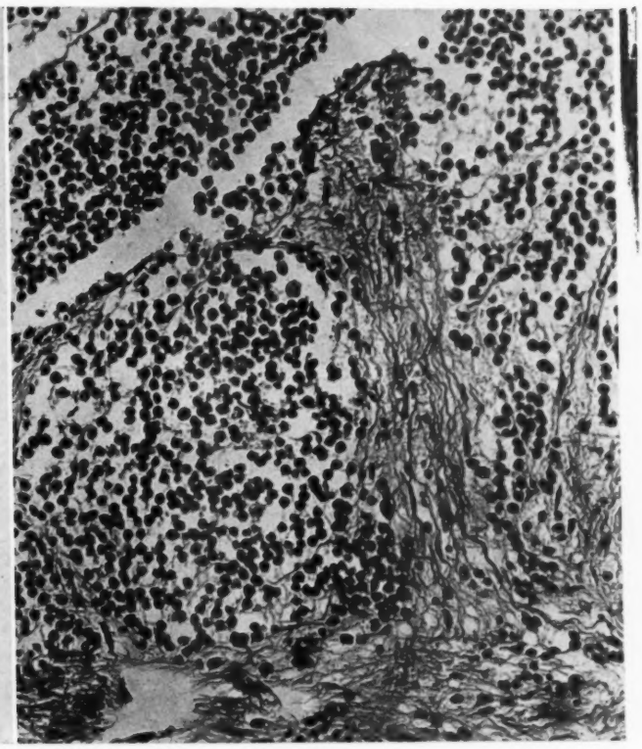

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FIG. 7. Same case. Low power view of the nodule shown in Figure 6.

FIG. 8. Same case. Higher power view of the primary malignant melanoma shown in Figure 7.

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FIG. 9. Same case. Recurrence and massive axillary metastasis four months after excision of the primary malignant melanoma.

FIG. 10. Same case. The axillary and suprascapular mass.

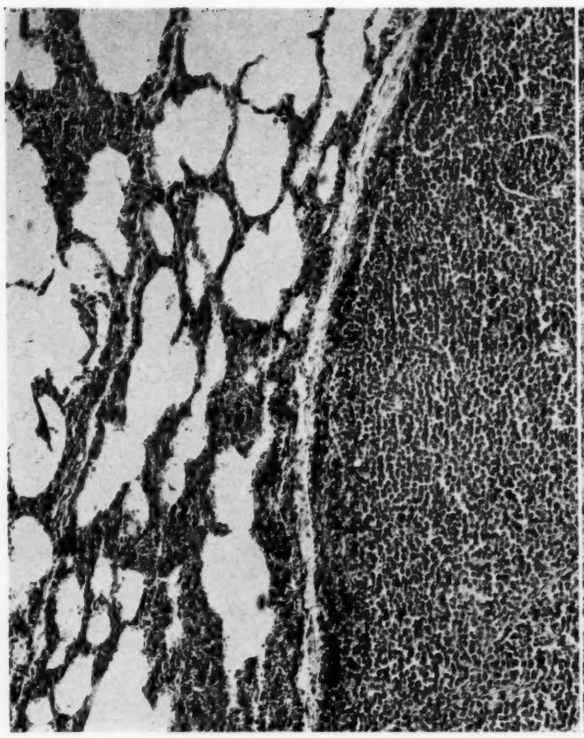

FIG. 11. Same case. Metastatic melanoma in the lung.

FIG. 12. Same case. Metastatic melanoma in kidney.

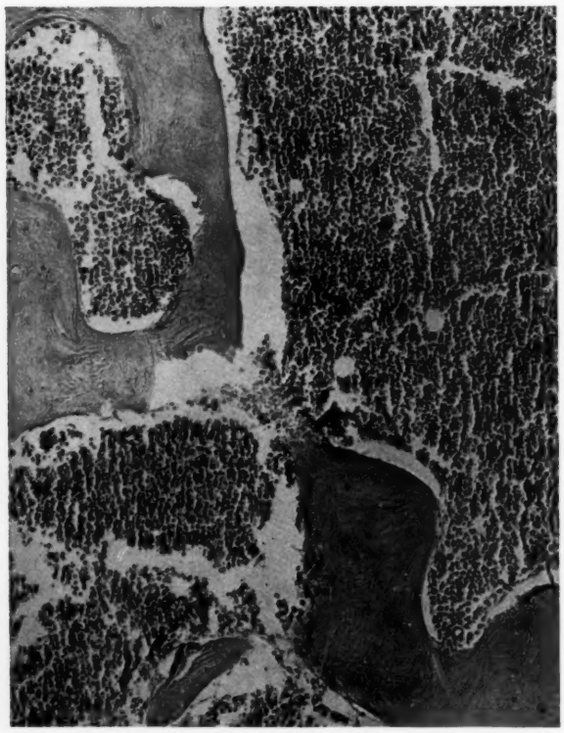

FIG. 13. Same case. Metastasis in femur.

July 18, 1953. Autopsy on July 19th showed very extensive metastases.

The anatomic diagnosis was summarized as follows:

"1. Nevus, back, congenital, hairy. 2. Melanoma, thoracic wall, massive; (a) melanoma, metastatic, axillary nodes; (b) melanoma, metastatic, lungs (Fig. 11); (c) melanoma, metastatic, brain; (d) melanoma, metastatic, skull; (e) melanoma, metastatic, liver; (f) melanoma, metastatic, kidneys (Fig. 12); (g) melanoma, metastatic, ovary; (h) melanoma, metastatic, femur (Fig. 13); (i) melanoma, metastatic, pericardium."

The pathologist added this note: "The tumor looks very much like it did in the original surgical specimen. Many metastases are markedly pigmented. In others, the pigment occurs mainly in necrotic areas. There is not an unusual amount of necrosis for a tumor of this degree of malignancy and mitoses are numerous."

*Comment.* A malignant melanoma developed in a congenital giant compound nevus on the back of a two year old Negro girl. The growth

of the melanoma was apparently not affected by a full course of triethylene-phosphoramide (TEPA) or a short course of aminopterin. The tumor recurred, metastasized widely and caused the patient's death within seven months of the first excision. It would appear that this case is a compound rarity since the patient was under two years of age, a Negro, and malignant melanoma arose in a benign hairy nevus.

## PREPUBERTAL MALIGNANT MELANOMA

Malignant melanomas in children are rare, but they are not as unusual as they were considered to be five years ago. In 1948 Pack[2] pointed out that some children had skin lesions which looked like malignant melanomas, both clinically and histologically, and yet they did not metastasize and ran a benign course. He suggested that this group of tumors be called prepubertal melanomas. In 1951 Pack and Scharnagel[3] stated that in their experience with more than 1,050 verified cases of malignant melanoma, they had never observed a single instance in which melanoma of infancy or childhood had metastasized to nodes and viscera, and they had never witnessed a fatal outcome. In 1952 Pack[4] reported on 1,250 cases of malignant melanoma. He stated that even with the greater experience none of these melanotic tumors of infancy and childhood had metastasized to regional lymph nodes although many of them had been labelled as malignant melanomas by extremely competent pathologists. In this last report Pack[4] noted that there had been a few isolated instances in which metastases had occurred but he stated that it must be an extreme rarity.

There have been many reports emphasizing the benign course taken by melanomas in infancy and childhood.[5–9] These reports recognized the fact that in children melanomas may appear malignant histologically but not clinically. In 1948 Spitz[10] described the histologic characteristics of juvenile melanomas. In 1949 Allen[11] presented further histologic studies and speculated as to what happens to untreated juvenile melanomas.

In 1953 Allen and Spitz[12] reported their further studies on the histology of melanomas. They reported five cases of malignant melanomas in children, three of the cases being from New York Memorial Hospital. They described certain histologic differences between malignant and juvenile melanomas.

In recent years a number of malignant melanomas in children have been reported.[6,8,10,12–16] McWhorter and Woolner[16] studied all pigmented skin lesions removed from children twelve years of age or younger at the Mayo Clinic for the period from 1907 to 1949 and found five malignant melanomas. They reviewed the literature and accepted eighteen cases as being authentic. They did not include the cases of Coffey and Berkeley[13] or Williams[15] although these were included in a later article.[23]

McWhorter and Woolner[16] pointed out that the good prognosis accorded "malignant melanomas" in childhood was because in the earlier literature benign juvenile melanomas and rare malignant melanomas had been grouped together.

From a study of reported malignant melanomas in childhood it is apparent that these tumors behave like malignant melanomas in adults except that the prognosis is worse in children. Of the eighteen cases accepted by McWhorter and Wollner[16] as authentic, only two had lived more than five years.

## TREATMENT

On the basis of the clinical appearance alone it is usually impossible to differentiate malignant melanoma from juvenile melanoma, or even at times from an active junctional nevus. It is important, therefore, to have a high index of suspicion and to think of the possibility of malignancy in any rapidly growing, easily traumatized or ulcerated lesion, deeply pigmented or not, which does not improve within two weeks on the usual protective treatment. The lesion should be excised with a margin and then examined microscopically. If the lesion is a junctional nevus or juvenile melanoma, no further treatment is needed. If it is malignant melanoma, a radically wide local excision, usually requiring a skin graft, should be performed.

It has been emphasized repeatedly that malignant melanomas in children should be treated as radically as those in adults.[12,16,23] On the basis of the study of cases of malignant melanoma in the Stanford Tumor Clinic and the Letterman Army Hospital,[1] and after reviewing the literature on the subject, we concluded that a radical block regional lymph node dissection should be performed in every case

without distant metastases, *whether the nodes are enlarged or not.* If the primary tumor is near the regional lymph nodes, the local excision and node dissection should be done in continuity, as first described by Pringle[24] and later advocated by Pack.[25] In 1953[1] we presented certain arguments supporting prophylactic lymph dissection, and further experience has strengthened that opinion. We are opposed to taking a biopsy of melanomas and are of the opinion that they should always be excised for microscopic examination.

### MALIGNANT MELANOMA ARISING IN GIANT HAIRY NEVI

Congenital giant hairy nevi have been thought to be benign, safe lesions. These unsightly lesions have been considered to be so innocuous that they have been freely cauterized, excised piecemeal or removed in layers with a dermatome. The usual method for the removal of the smaller lesions has been full-thickness excision and the closure of the defect with flaps or split-skin grafts. Most of the giant nevi are so large that the excision has to be done in multiple stages, suturing the defect at each procedure. Pickrell et al.[17] and Greeley[18] favor serial or multiple segmental excisions. In 1953 Cronin[19] reported the use of the dermatome to remove pigmented areas in the upper dermis while preserving the hair follicles in normal hair-bearing areas. He discussed the possibility of this method producing malignant change in a nevus and concluded that this method should not be used in junctional nevi in adults but would probably be safe in children prior to puberty.

In addition to Case II reported herein there have been other cases of malignant melanomas arising before puberty in giant hairy nevi. In 1939 Conway[20] collected forty cases of bathing trunk nevi and found one case reported by Jablokoff and Klein[21] in 1879. This was a six and a half month old girl in whom malignant melanoma developed within the area of a bathing trunk nevus. Death resulted from multiple melanotic metastases in the brain. In 1939 Pack and Anglem[5] first described the case of a baby girl with an extensive congenital melanotic nevus who was first examined in 1935 at five and a half months of age. Over a period of several years nineteen tumors were excised from the nevus; all were said to be prepubertal melanomas. In 1936 a left kidney tumor was removed and diagnosed as embryonal adenocarcinoma. In 1952 Pack, Scharnagel and Hillyer[22] gave the follow-up report on the case. There were no new tumors or metastases for fifteen years. In 1951 signs suggesting a brain tumor developed and at craniotomy metastatic melanoma was found. In 1954 Williams[15] reported the case of a two year old white girl. She was first seen in 1935 with extensive confluent, hairy, pigmented lesions of the neck, thorax and arms. Eighteen months later a mass had developed within the nevus on her left upper arm. When excised the mass was found to be malignant melanoma. Widespread metastases produced death within eight months. Two separate foci of malignant melanoma were found. In 1954 McWhorter and Woolner[16] reported the case of an eight year old boy who had had a large, hairy, pigmented mole on the right cheek and ear since birth. A nodule developed in the nevus and the entire area was excised and neck dissection performed. The mole was a benign compound nevus and there were three separate foci of malignant melanoma.

Case II reported herein is the fifth case found in the literature in which malignant melanoma has developed in a congenital benign hairy nevus. All five patients died. In three and possibly four of the cases there were multiple foci.

### SUMMARY AND CONCLUSIONS

1. Two cases of malignant melanoma of the skin in children are reported.

2. Malignant melanomas in children are rare but they are not as uncommon as they were considered to be five years ago.

3. Malignant melanomas in children can usually be differentiated histologically from juvenile melanomas and should be treated as radically as adult malignant melanomas. This includes a radically wide local excision with skin grafting and a radical block dissection of the regional lymph nodes, *whether the nodes are enlarged or not.* The local excision and node dissection should be done in continuity whenever feasible.

4. The prognosis of true malignant melanomas in children is worse than in adult melanomas.

5. Congenital giant hairy nevi have been considered to be innocuous and have usually been removed leisurely and piecemeal for cosmetic reasons. At least four cases of malig-

nant melanomas arising in benign giant hairy nevi have previously been reported. Case 11 reported herein is an additional case. Three of the five had multiple malignant foci.

6. Since congenital giant hairy nevi may undergo malignant changes it is advisable to remove them as early and as completely as possible. They should be followed regularly and widely excised at the earliest sign of malignant change.

7. The possibility of malignant melanomas in children should be considered in growing nodular or ulcerated skin lesions, pigmented or not, which do not heal in two or three weeks with usual therapy.

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# Gastric Resection

## A COMPILATION OF TECHNICS

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MANY excellent treatises on surgical treatment of peptic ulcer have been published by clinical and experimental workers who generally agree that there are two fundamental elements necessary for satisfactory gastric resection; namely, adequate resection and an anastomosis so arranged that the stoma is quickly bathed in the alkaline biliary and pancreatic juices. Points of argument revolve around the size of the stoma, the direction of the intestinal loop, whether it should be in front of or behind the large bowel, and the various methods of closure of the duodenal stump. Adequate resection with direct end-to-end gastroduodenal anastomosis fulfills the requirements and obviates most of the problems. In addition, the more normal anatomy of the gastrointestinal tract apparently is compatible with a more normal physiology. The direct entrance of food into the duodenum produces a greater stimulation of pancreatic and biliary secretion with better mixing of food with the secretion and consequently an improved fat and protein assimilation.[1,2] In addition, several authors believe that iron absorption, which is most active in the duodenum, is improved by the simultaneous administration of fat and is assisted by the presence of bile.[3]

For these reasons, the last forty gastric resections which my colleague or I performed for peptic ulcer in the last four years were of the Billroth I variety. In six of these we used a Finney-von Haberer modification employing an end-to-side gastroduodenostomy. This was done because either there was insufficient posterior duodenal wall available for anastomosis after the ulcer was resected, the adjacent area was too edematous, or we wished to avoid a mechanical block such as was present in the case of annular pancreas reported in this issue by Dr. F. P. Shidler. On one occasion, we could not perform gastroduodenostomy after adequate resection because the patient was extremely obese and a mountain of retroperitoneal fat combined with the weight of the huge greater omentum put too much tension on the site of anastomosis. The procedure is ordinarily performed as an open operation. This requires less duodenal wall than is necessary when a clamp is applied for a closed anastomosis and it does not necessitate the invagination of any crushed or devitalized tissue into a small stoma. Anastomosis is performed between the duodenum and either the lesser or greater curvature side of the cut end of the stomach. In the usual case the greater curvature side is employed. Occasionally, however, if the stomach has a large fundus, the greater curvature side is freed completely and the clamps are so applied that 2 inches of the lesser curvature below the cardia are left and all the greater curvature is resected, using the lesser curvature side for the anastomosis. Employing a modification of the method Dr. Holman often uses for opening the bowel,[4] an incision is then made through the serosa and muscularis of the stomach just proximal to the Payr clamps, down to the submucosal vessels. These are then coagulated with the electrocautery until the contracture of this layer draws the clamp back to within 2 or 3 mm. of the previously retracted muscularis and serosa. On the side of the stomach to be closed, a continuous No. 00 chromic catgut suture is then run back and forth from the anterior to posterior stomach walls under the clamp at the edge of the serosa. The devitalized cuff of stomach tissue contained in the clamp and most of the coagulated wall is then cut off and any small bleeding point not secured by the hemostatic suture may be readily coagulated. (Fig. 1.) This portion of the stomach is then closed by returning the suture to the starting point as a continuous Connell suture which is then reinforced with interrupted Lembert or Halsted sutures of No. 0000 cotton. These extra precautions at hemostasis were taken because on several occasions a large amount of blood was found

within the stomach and once the closure had to be taken apart to control the bleeding. In this patient, a fairly large intramural hematoma developed, to which we attribute the fact that his stomach took two or three weeks to empty satisfactorily instead of two or three days. Since employing this method, we have been impressed by the small amount of bleeding encountered at surgery or afterward through the nasogastric tube. The wall of the stomach to be used for the anastomosis is similarly cauterized and the crushed portion excised. Anastomosis is accomplished in two layers, beginning with a continuous Connell suture in the mid-portion of the posterior wall which is later reinforced with interrupted Halsted sutures of cotton. This inner suture allows the external cotton sutures to be smaller and more meticulously placed, minimizing the amount of tissue invaginated, and is therefore done before the posterior row of cotton sutures is inserted. However, when the duodenal cuff is too short to permit adequate rotation, the external posterior row of sutures may be placed as the inner catgut suture progresses along the posterior wall so that rotation will not be necessary at completion of the inner suture.

It probably is not wise to place a new anastomosis in an area of dense scarring or more acute reaction. However, we believe there is no basis for either the old objection to the Billroth 1, namely, leakage at the "fatal angle," or the recent objection that an adequate resection cannot be performed. Careful approximation of good serosal layers will prevent leaks and, naturally, resection is performed before anastomosis and therefore the latter cannot determine the proper extent of the former. With adequate mobilization the duodenum can be brought up to approximate the lower esophagus if necessary, and rarely will it be impossible to perform gastroduodenal anastomosis. One of the chief advantages of being persistent in performing a Billroth 1 operation is that one acquires more assurance in working on this portion of the duodenum and will be less inclined to leave behind the ulcers that seem difficult to resect. In addition, on several occasions, when there was insufficient posterior duodenal wall available for a satisfactory suture line, the end-to-side gastroduodenostomy worked out well. This latter procedure offers a vent near the site of the duodenal closure which in turn will not be subjected to back pressure from a possible short loop obstruction.

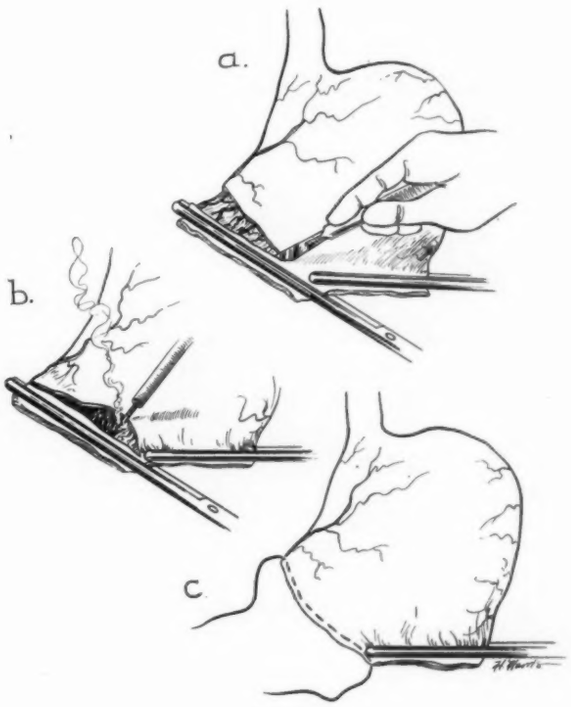


FIG. 1.

The only conclusions to be drawn from such a small series of patients is that this is a satisfactory procedure which can be done safely without a significant number of postoperative ill effects.

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# Surgical Treatment of Coarctation of the Aorta in Infancy

## REPORT OF TWO CASES

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THE surgical treatment of coarctation of the aorta has now become established on a firm basis. We advise operation between the ages of ten and twenty years with little regard for the absence of symptoms. There are few patients beyond this age who do not have either hypertension or symptoms, and therefore the majority of the patients who fall into this older age group are automatically accepted for operation.

The importance of this lesion as a common cause of cardiac death under two years of age was stressed by Calodney and Carsen,[1] Bahn and his associates,[2] and others.[3–5] Although it was formerly held that it was the combination of this lesion with other congenital cardiac defects which was responsible for the grave outlook,[6] their studies showed that in the majority of the instances coarctation alone could have been responsible for the cardiac failure. Two types of coarctation are generally described: (1) The adult type, in which the involved aorta is of near normal size, a sharp constriction is present and the ductal lumen is small or closed. In this type there is generally a good collateral circulation which developed during fetal life and the prognosis is favorable. (2) The infantile type, in which the proximal aorta is diffusely narrowed and there is frequently an associated patent ductus which enters the aorta distal to the coarctation; the collateral circulation does not develop until after birth, and then to a lesser degree than in the adult type. This anomaly is poorly tolerated, and frequently results in early death. Often elements of both types are present in a single individual.

The differential diagnosis may be difficult, but one should consider the possibility that coarctation may be present in any infant who shows signs of cardiac failure early. Manifestations in infancy are rapid, grunting respirations, tachycardia, cardiac enlargement and a murmur. Edema and hepatomegaly may also be present. Cyanosis, when present, may stem either from the associated anomalies or from congestive heart failure. Full, bounding brachial pulse, elevated arm blood pressures and weak femoral pulses are constant findings. If the coarctation is preductile, venous blood is supplied by the right ventricle through the ductus to the descending aorta. The toes may be blue while the fingers are pink, although the presence of congestive failure confuses this differential sign. Roentgenograms show cardiomegaly. Aortagrams, made by injecting radiopaque material retrograde into the left brachial artery, will show the nature and extent of the coarctation,[7] but since there are hazards in using this procedure in the seriously ill infant, it should not be employed routinely. It is important to remember that the electrocardiogram may show right, left or no ventricular preponderance.

Question has arisen over the advisability of operating upon those infants and young children with aortic coarctation in whom alarming symptoms have developed. This stems from uncertainty concerning the continued growth of the area of anastomosis. However, experimental data have shown that enlargement will take place in growing animals and it is therefore likely that the vessel wall in this area will continue to stretch and grow and that the lumen will remain adequate.[8] In any event the immediate problem in these infants is a surgically amenable, mechanical one causing urgent cardiac failure.

Several communications on surgical repair of coarctation in infancy have appeared. Kirklin and associates reported a successful operation upon a ten-week old infant who was in good clinical condition eighteen months after operation.[9] Sealy and Webb operated upon a sixteen-month old child, with sustained improvement after two and a half years.[10] Olney and Stephens described a number of instances of cardiac failure due to coarctation in the younger age group and advocated early operation under these circumstances.[11]

It has been our policy to make every effort to maintain these infants and young children on a medical regimen as long as possible, and in most instances it is feasible to do this until a more optimal age for operation is reached. However, some will not survive despite the best of conservative measures and for these operation is the only hope.

During the past few years we have used hypothermia as an adjunct to cardiac operations on severely cyanotic children and on a selected number of infants in whom non-cyanotic, congenital, cardiovascular abnormalities had produced congestive heart failure.[12–14]

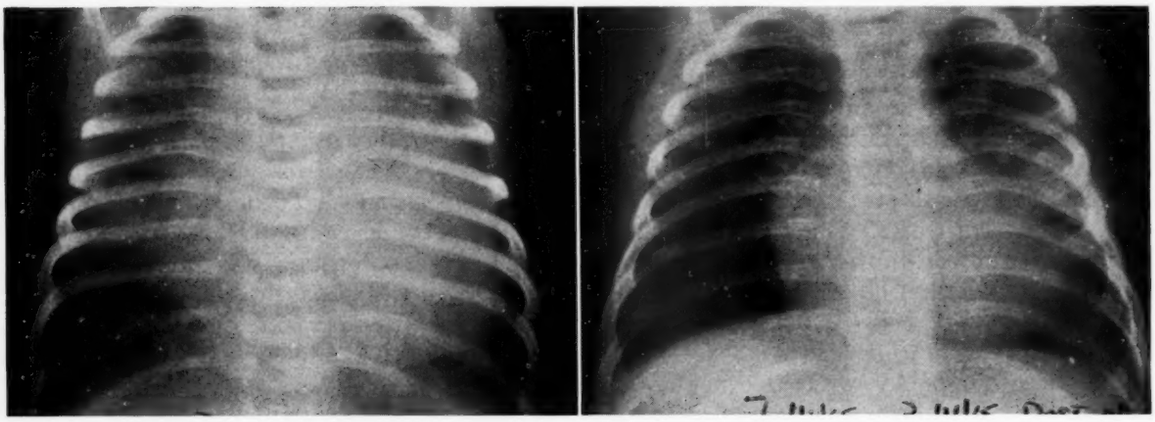
In this combined group there were twelve who were seriously ill and who were operated upon at an early age as the only hope of preventing death. Temperatures were reduced to 31°c. by surface cooling with cracked ice in plastic bags. This was usually followed by a further 3 or 4 degree spontaneous drop in rectal temperature. Nine of these patients had extracardiac procedures and three, intracardiac. There were no complications which could be attributed to the hypothermia. Eight patients are alive, either cured or improved, and four died. Death in three of these children was due to anatomic defects that could not be corrected. The fourth patient, who had extreme, pure valvular, pulmonary stenosis, had long been in intractable congestive failure; he had a left heart too small to turn over the greatly increased amount of blood suddenly returned to it through a freely open pulmonary valve and died in acute pulmonary congestion on the second postoperative day. In all of these infants the heart rate was slow, the arterial oxygen saturation remained high, a minimal amount of anesthetic reagent was required and the operative procedure was made easier by hypothermia.

It is the purpose of this paper to report successful coarctation operations on two infants, one of whom is included in this group of twelve. This was a three-month old infant with an infantile, preductile type of coarctation, a large patent ductus arteriosus and an intracardiac shunt. The second was a one-month old infant who had an adult type of coarctation. Both patients were in congestive heart failure. Repair of the coarctation was rather easily accomplished, and it was our impression that the reduced body temperature, used in one patient, was an operative aid.

### CASE REPORTS

CASE 1. D. M., a male child, was born on April 2, 1952. He weighed 7 and $\frac{3}{16}$ pounds and appeared to be perfectly normal. Ten days after birth choking spells and regurgitation of food began. For these he entered the hospital. Studies there revealed a density in the right middle lobe, a marked cardiac enlargement and a prominence of the pulmonary vessels. A Grade III systolic murmur was heard over the precordium and the electrocardiogram showed signs of right ventricular enlargement. A retrograde, brachial aortagram demonstrated a coarctation. Subsequent to this procedure his course was that of cardiac failure with cyanosis (whenever out of oxygen), moist pulmonary rales and enlargement of the liver. He was maintained on 0.015 mg. of digitoxin a day and transferred to Stanford University Hospital on May 1, 1952. On admission the blood pressure in his right arm was approximately 180 mm. Hg, in the left arm 170 mm. Hg and unobtainable in the legs. No murmurs were heard. Since his course had progressively worsened despite good medical treatment, operation was recommended and performed on May 3, 1952.

Using ether and oxygen anesthesia, the thorax was opened in the fourth interspace. A large number of collateral vessels were found. The coarctation was exposed and the arch and the distal aorta were fully mobilized. The ductus was patent at the aortic end. Patency at the pulmonic end was not determined. A Potts clamp, serrated type, was placed across the distal aorta, another proximal to the left subclavian artery, and a ligature was tied over a rubber pad to occlude the left subclavian artery. The first intercostal artery was tied. The coarctation was resected and the ductus ligated on the pulmonary side. At the site of the coarctation the aortic lumen was only 1 mm.



1A 1B

1C

FIGS. 1A and B. Case 1. Roentgenograms showing the size of heart and pulmonary congestion resulting from an adult type of coarctation. A, at three weeks. B, at seven weeks, three weeks postoperative.

FIG. 1C. Case 1. Seven months after repair the heart size was nearly normal.

in diameter. A lumen of approximately 6 to 7 mm. in diameter was established by an anastomosis consisting of a posterior row of everting, continuous sutures and an anterior row of four everting, mattress sutures of No. ooooo silk. Underwater sealed drainage was established. The postoperative course was uneventful. The drain was removed on the second day. Good femoral and dorsalis pedis pulses were felt throughout the postoperative period. The patient was dismissed on the eighteenth postoperative day, at which time roentgenograms showed a decrease in the cardiac silhouette. (Fig. 1.) Since then there has been normal growth and development. Examination on April 3, 1954, revealed a healthy, vigorous child who weighed 29 pounds and was 35½ inches in length. The blood pressure in the right arm was 110/80 mm. Hg, in the right leg 90/60 mm. Hg, and good femoral and pedal pulses were present. A soft, systolic murmur was present. On September 24, 1954, growth had progressed normally and the pressures were: right arm 114/80, left arm 130/90, right leg 110/80.

CASE II. S. C., a Caucasian female infant, was admitted to the Children's Hospital for the first time at the age of three weeks. Her weight at birth, March 14, 1953, had been 5 and $^{11}/_{16}$ pounds. Since birth the mother had noticed rapid respirations and regurgitation of food once or twice a day. On the day of admission she had an episode of marked pallor, requiring the administration of oxygen. Physical examination on admission revealed the infant to be in acute distress and weighing 6 and $^{3}/_{16}$ pounds. The respiratory rate was 66 per minute. The left hemithorax was more prominent than the right. There were inspiratory rales in both bases. The heart rate at the apex was 180 per minute with a regular rhythm. The left cardiac border was in the anterior axillary line. There was a Grade II systolic murmur along the left sternal border.

The femoral pulses were palpable but very weak. The liver and spleen were not enlarged. The flush blood pressure of the left arm was approximately 155 mm. Hg; right arm 140; left leg 45; and right leg 40. The electrocardiogram showed auricular and right ventricular hypertrophy. Roentgen examination of the thorax revealed a cardiothoracic ratio of .70, right sided predominance, with fullness of the pulmonary artery and vascular markings.

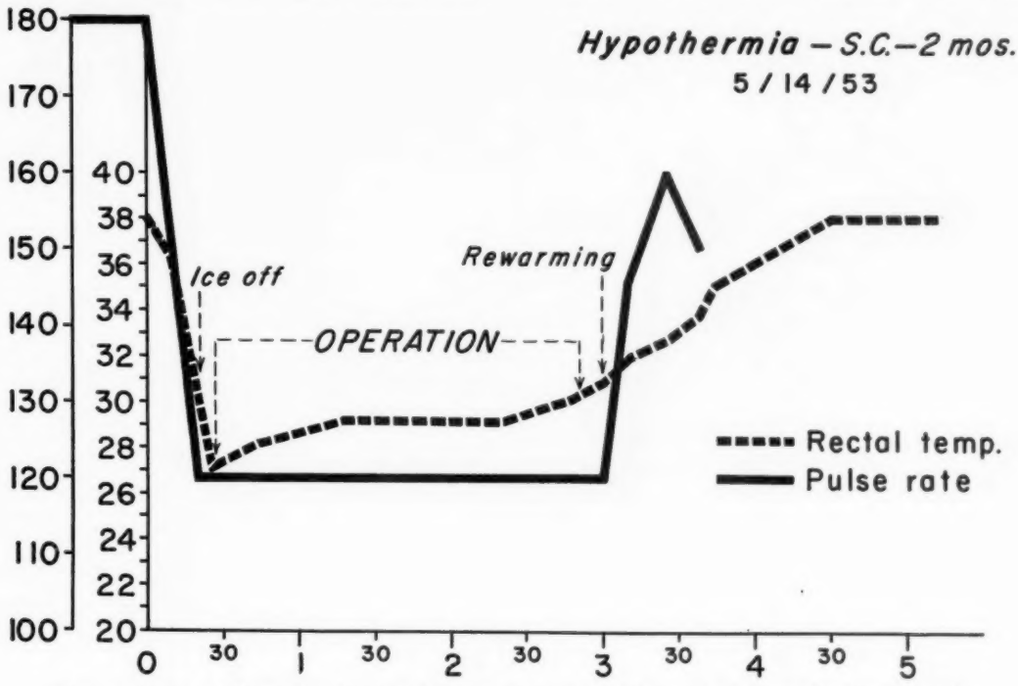



FIG. 2. Case 11. Chart showing the fall in pulse rate which resulted from the hypothermia.

Because of marked dyspnea and cyanosis it was necessary to keep the infant in oxygen. Due to inability to eat, tube feeding was started on April 19, 1953. She was given digitalis with no demonstrable improvement. Antibiotics were used to rule out pulmonary infectious disease as a contributory factor to heart failure, but also without improvement. Episodes of marked dyspnea and pallor became more frequent, and the liver enlarged to 4 cm. below the right costal margin. Preoperative physical examination at two months of age showed a weight of 6 and $9/16$ pounds (a 14 ounce gain over her birth weight), cardiac border 4.5 cm. to the left of the midsternal line, a Grade III to IV systolic murmur maximum at the left midsternal border, a heart rate of 140, absence of femoral pulses and no difference in the color of the hands and feet. Five minutes out of oxygen produced an increasing tachypnea, intercostal and suprasternal retraction, cyanosis of the lips and fullness of the neck veins. Because of the failure of all therapy, operation was recommended.

Operation was performed on May 14, 1953. The infant received $1/400$ gr. of atropine sulphate before operation and light anesthesia was established with ether and oxygen. Hypothermia was then induced by enveloping the infant with cracked ice in plastic bags. The initial rectal temperature was 38°C. and in twenty minutes it fell to 29.5°C. at which point the ice was removed. Thereafter the temperature fell to 27°C. where it remained during the operation. After inducing hypothermia only oxygen was given. (Fig. 2.)

The thorax was opened through a posterolateral incision in the fourth interspace. There was very little bleeding and no enlarged collaterals were seen. Dissection revealed a coarctation of the aorta with hypoplasia of the proximal portion of the aorta (4 mm. in diameter) which swung up sharply to a left subclavian artery which was 3 to 4 mm. in diameter. Beyond the coarctation a ductus measuring 7 mm. in diameter entered the distal aorta. The aorta could be mobilized without sacrifice of any intercostal vessels, and it was possible to gain considerable length by freeing the proximal aorta. Resection of the coarcted seg-

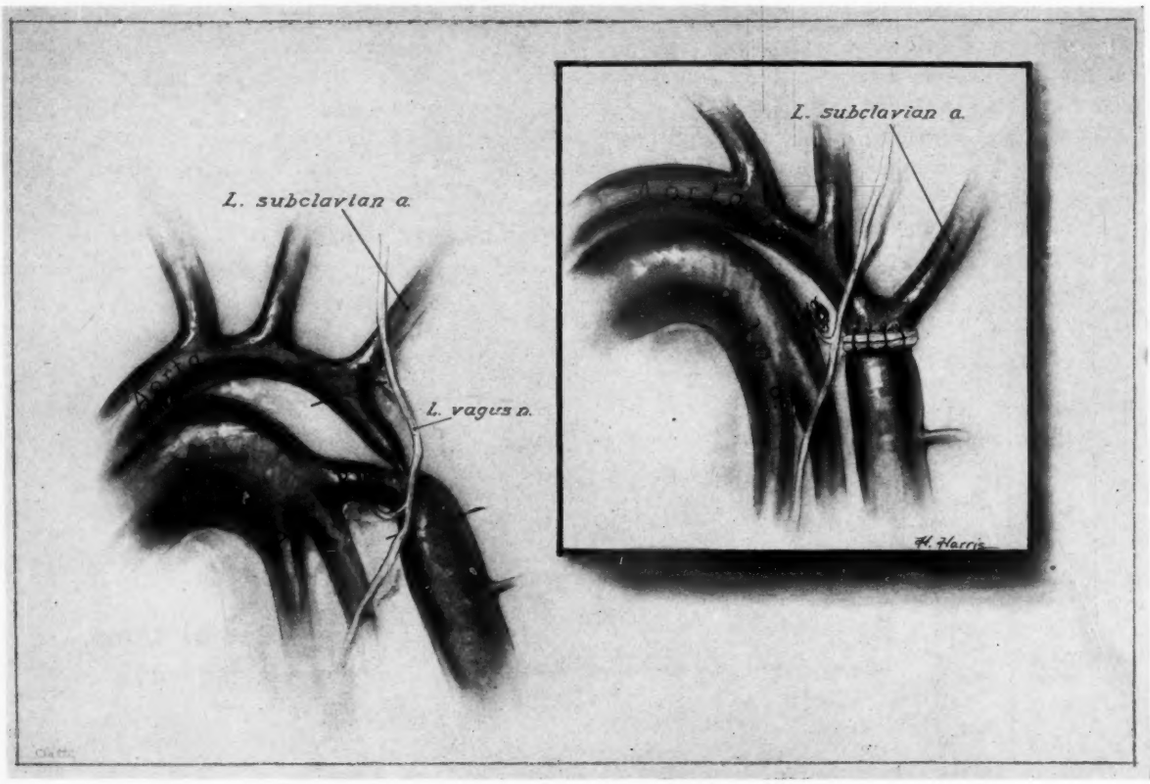



FIG. 3. Case 11. Anatomic findings and operative result obtained. Full mobilization of the proximal aorta and subclavian artery made it possible to perform anastomosis despite the length of segment removed.

ment was performed, with closure of the pulmonary side of the ductus by double ligature. An end-to-end anastomosis was done with a continuous, over-and-over suture in the posterior row and interrupted, everting, mattress sutures anteriorly. A good pulsation was felt in the distal aorta after the clamps were removed. Underwater sealed drainage was established. Digitoxin was continued postoperatively. (Fig. 3.)

Tube feeding was started on the second postoperative day and mouth feeding on the fourth. After the second day the child was pink when out of the oxygen, and respirations were effortless and regular. On the tenth postoperative day the flush blood pressures in both right arm and leg were 118 mm. Hg. A loud, systolic murmur was still heard in the second and third left interspaces at LSB; the liver was 2.5 cm. below the costal margin. The patient was receiving 0.016 mg. of digitoxin daily when she left the hospital on the thirteenth postoperative day.

On July 1, 1953, the patient re-entered the hospital for a follow-up study. The parents had noticed progressive improvement since leaving the hospital, although a cough and some rapid breathing were still occasionally present. The pulse rate was 130 and the respirations 24. There were good femoral and pedal pulses. Roentgenograms of the thorax revealed a decrease of approximately 15 per cent of the cardiac shadow. Electrocardiogram showed less evidence of digitalis effect and a decrease in the right ventricular hypertrophy. She was still taking 0.016 mg. of digitoxin per day. A Grade III systolic murmur was heard best at the aortic and pulmonic areas. The lungs were clear. In October, 1953, further improvement was noted, growth had progressed normally and feeding was no longer a problem. Good femoral and pedal pulses were present, the blood pressures in both arms were 100/75 mm. Hg and by the flush method in the legs, 90 mm. Hg. In October, 1954, the child's progress continued to be satisfactory.

## SUMMARY

1. One infant with heart failure due to an adult type of coarctation was operated upon successfully at the age of one month, and after twenty-nine months satisfactory lowering of

arm pressures and good leg pressures have been maintained.

2. One infant with heart failure was operated upon successfully under hypothermia at the age of two months for an infantile type of coarctation with a large ductus emptying into the aorta beyond the constriction. There was also an associated septal defect which has not been treated. A satisfactory circulatory status has remained for the seventeen months following operation.

3. Hypothermia may be a useful adjunct to cardiovascular procedures in infants.

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# Unilateral Exophthalmos Due to Orbitofrontal Cholesterol Granuloma

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WE have recently had the opportunity to study two cases of unilateral exophthalmos due to the same type of orbitofrontal destructive lesion. A similar case has been found in the files of the Montreal Neurological Institute and the pathologic material has been restudied. One of us (J. H.) studied an additional case which was included in an earlier report[1] of twelve orbital tumors. The pathologic material from this case has been reexamined, found to be the same as the other three cases and has been included in this series (Case II).

The clinical, radiologic and pathologic aspects of these four cases are practically identical. We have found five other reported cases which also seem to represent the same disease process. The purpose of this report is to (1) summarize the clinical and pathologic features of these nine cases, (2) discuss the differential diagnosis, (3) record our interpretation of the lesion and (4) make certain recommendations regarding therapy.

## CASE REPORTS

CASE I.* This fifty-seven year old man was admitted to the Montreal Neurological Institute in July, 1944, complaining of a right supraorbital swelling and dizziness. In 1919 he had been struck on the right supraorbital ridge by a flying spike, and sometime later developed a small, painless, persistent swelling in this region. He entered the Montreal General Hospital in November, 1943, after being struck by an automobile. There was evidence of recent injury about the right orbit, and at certain points over the superior orbital margin the bone could be compressed and crepitus was present. There was prominence of the right eye and limitation of upward movement. X-rays showed a comminuted fracture of the lateral and superior margins of the right orbit with lateral displacement of the fragments. A biopsy was performed. The patient failed to return. About six months later the supraorbital mass began to enlarge rapidly and he was referred to this hospital.

Examination revealed a firm, irregular, reddish swelling over the lateral margin of the right supraorbital ridge which was continuous with the frontal bone. (Fig. 1.) There was unilateral exophthalmos with downward and medial displacement of the globe, and diplopia. Visual fields and acuity were normal. No abnormalities were noted on examination of the fundus.

Blood serology was negative. Serum cholesterol levels were not determined. X-rays showed a rarefied area 3.5 by 3.8 cm. involving the lateral three-fourths of the right supraorbital ridge. The margins of the defect were fairly distinct, and the lesion did not communicate with the frontal or ethmoid sinuses. A large portion of the orbital roof was involved.

On July 28, 1944, the lesion was exposed by Dr. G. Morton by reflecting anteriorly a right frontal scalp flap. A craniotomy was not performed, but the lesion was excised after removing what remained of the supraorbital ridge. A partially cystic lesion was found extending from the frontal bone into the adjacent portion of the zygomatic process and destroyed a portion of the orbital roof. There was a considerable intraorbital extension which was adherent to the lacrimal gland and displaced the globe forward, downward and medially, but had not penetrated the orbital fascia or dura. The abnormal tissue was soft, brownish, avascular and contained cysts filled with a yellowish, glistening, gelatinous material. A large supra-

* This case was included in the report by Ramsey et al.[2] in 1948 and was the first of the two patients which they described. The case has been added to this series with the permission of the original authors.

orbital defect was left without attempting a plastic repair.

The patient's postoperative recovery was uneventful and his symptoms subsided. When last seen three years later, he had no evidence of recurrence.

CASE II. A thirty-one year old man entered the Stanford University ophthalmology clinic in January, 1945, complaining of diplopia and pain over his right eye of two months' duration. The diplopia had first occurred eighteen months previously. Another physician had found no intrinsic eye disturbance, but

FIG. 1. Case I. Firm, irregular, reddish swelling over the lateral margin of the right supraorbital ridge with forward, inferior and medial displacement of the eye.

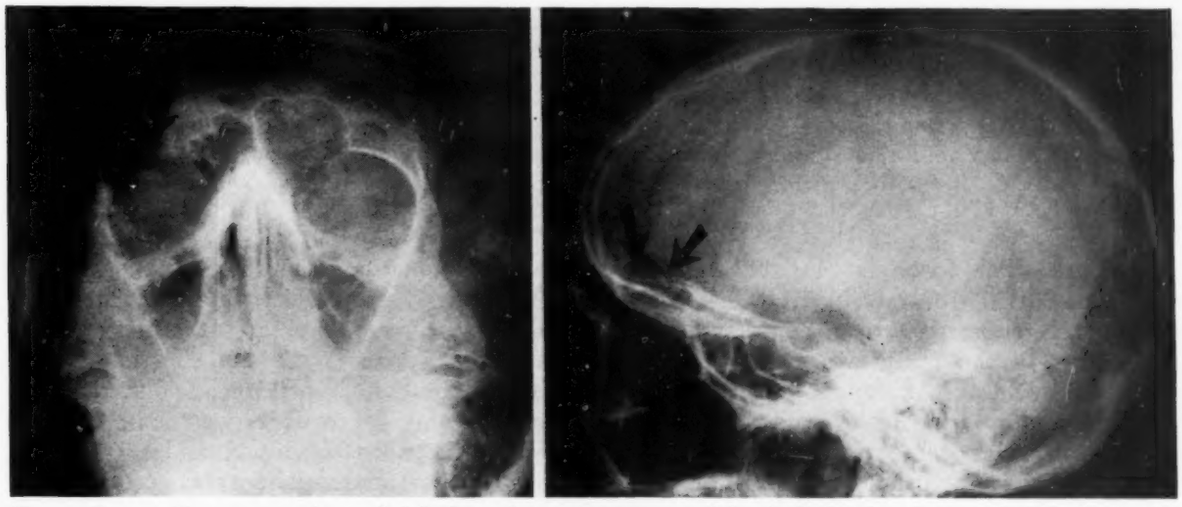

FIG. 2. Case II. Postero-anterior and right lateral roentgenograms of the skull showing the osteolytic lesion in the right supraorbital ridge, frontal squama and orbital roof.

because of slight proptosis had advised x-rays of the skull. This examination revealed "a bony growth behind the right eye," and he was given a course of x-ray therapy (6,000 roentgens) to the right orbital region. There was moderate regression of proptosis, the diplopia disappeared and he was entirely asymptomatic until two months prior to admission. There was no history of trauma.

Examination revealed a unilateral exophthalmos of 4.5 mm. Visual acuity, fundi and visual fields were normal. The globe was slightly displaced downward and medially and diplopia was present. There was no visible or palpable abnormality of the supraorbital ridge.

X-ray examination showed a rounded defect measuring 2.5 by 1.5 cm. in the lateral portion of the right supraorbital ridge involving the frontal squama as well as a portion of the orbital roof. (Fig. 2.) There was no leukocytosis or eosinophilia. Blood serology was negative. Serum cholesterol levels of 195 mg. per cent and 178 mg. per cent were obtained postoperatively.

Dr. F. L. Reichert operated upon the patient in March, 1945. A right frontal craniotomy was performed, exposing the floor of the anterior fossa extradurally. An elevated area was found in the anterolateral portion of the orbital roof which was covered by greatly thinned, almost transparent bone. This was opened and orange-colored, soft, amorphous, gritty material extruded under pressure. The abnormal tissue was curetted from the cavity which communicated with the orbit. The orbital fascia, however, was intact, and there had been no invasion of the orbital fat or extraocular muscles.

The patient recovered rapidly after surgery. The proptosis was no longer present. Local pain and diplopia rapidly improved and when last contacted approximately one year postoperatively he was asymptomatic.

FIG. 3. A, Case III. Frontal and oblique views of patient, showing slight forward and inferior displacement of the right eye. B, Case IV. Slight forward and inferior displacement of left eye.

CASE III. This forty-six year old man was admitted to the Montreal Neurological Institute on October 18, 1953, complaining of prominence of the right eye and diplopia of six weeks' duration. At the age of seven years he sustained a head injury and had a left frontal scalp laceration. A few weeks after first being aware of protrusion of his right eye he struck his right frontal region against a door.

Examination revealed that the lateral portion of the right supraorbital ridge was more prominent than the left. There was a right unilateral exophthalmos with slight downward displacement of the globe. (Fig. 3A.) A soft nodular swelling was palpable beneath the lateral portion of the right supraorbital ridge. There was slight edema of the eyelids and injection of the bulbar conjunctiva near the lateral canthus. Visual acuity and fields were normal. Examination of the fundi revealed no abnormalities. There was slight restriction of upward gaze. Diplopia occurred if he looked to the right and upward or to the left and upward.

No abnormality was found on examination of the peripheral blood. Blood serology was negative. Serum calcium, inorganic phosphorous, acid and alkaline phosphatase levels were all normal. A serum cholesterol level of 222 mg. per cent was found one week postoperatively. X-rays showed the base of the zygomatic process of the right frontal bone, and a portion of the zygomatic process itself, to have been expanded by a soft tissue mass in the diploe. The outer table was greatly thinned and displaced outward. The lateral portion of the orbital roof was thinned and displaced downward. In only a few areas was compact bone observed between the lesion and surrounding normal diploic spaces. There was no connection with the paranasal sinuses.

On October 22, 1953, Dr. W. Penfield exposed the lesion by reflecting a right frontal scalp flap. Over the lateral aspect of the right supraorbital ridge the bone was paper-thin and was cracked. When this was opened a small amount of dark liquid blood escaped, revealing a cavity filled with mustard-colored, soft, necrotic, amorphous material. The inner table of the frontal bone had been eroded, and about 1 sq. cm. of yellow-stained but intact dura was exposed. There was a 1 by 2 cm. opening in the orbital roof through which the contents of the cavity had extended, compressing and staining but not invading the orbital fascia. The adjacent frontal bone, zygomatic process, and orbital roof were removed until normal bony tissue was exposed. No plastic repair was attempted. Cultures of the soft yellow material proved to be sterile.

Postoperative recovery was rapid and complete. The exophthalmos and diplopia disappeared. The supraorbital bony defect was noticeable and may require plastic repair at a

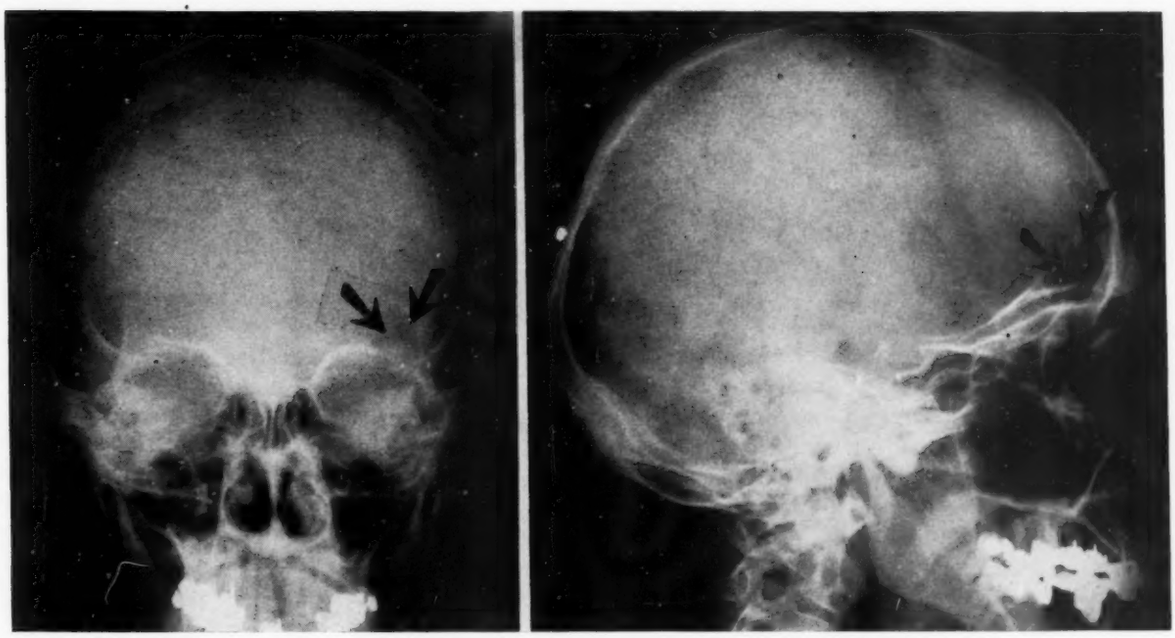

FIG. 4. Case IV. Postero-anterior and left lateral roentgenograms of the skull showing the osteolytic lesion in the left supraorbital ridge, frontal squama and orbital roof.

later date. He has remained well during the five months since operation.

CASE IV. This forty year old man entered the Montreal Neurological Institute on January 25, 1954, complaining of slight prominence of the left eye and diplopia of two weeks' duration. He had experienced no pain, headache or impaired visual acuity. He denied having sustained any injury to the left orbitofrontal region.

Upon examination there was no visible or palpable abnormality of the periorbital bony or soft tissues on the left side. There was a minimal left unilateral exophthalmos with slight downward and medial displacement of the globe. (Fig. 3B.) Diplopia was present only on gaze upward and to the left. Visual acuity, visual fields, pupils and fundi were normal.

Examination of the peripheral blood revealed no abnormality. The sedimentation rate was only 4 mm. per hour. Blood serology was negative. Serum proteins, inorganic phosphorous, acid and alkaline phosphatase levels were all within normal limits. Serum cholesterol was 245 mg. per cent. X-rays of the skull showed an area of destruction involving the lateral one-half of the left supraorbital ridge and adjacent portions of the frontal squama and orbital roof. (Fig. 4.) This discrete lesion was surrounded by an intact thin layer of compact bone. There was no relation to the paranasal sinuses.

On January 29, 1954, the patient was operated upon by Dr. W. Penfield, who exposed the lesion through a lateral eyebrow incision. The anterior portion of the temporalis fascia and muscle were mobilized and retracted backward. Two areas of marked bony thinning were noted, one in the frontal squama just above the lateral portion of the supraorbital ridge and another in the frontal bone just behind its zygomatic process within the temporal fossa. The abnormal bone was paper-thin and appeared blue and yellow. The cavity in the bone was entered through the area of thinning in the anterior portion of the temporal fossa and a small amount of dark blood escaped. The cavity was filled with a soft yellowish-brown, amorphous, gritty material. There was no capsule separating this substance from the eroded bony margins. A small amount of oily fluid containing crystals was found. Most of the roof of the orbit had been destroyed, and the contents of the cavity were in contact with the orbital fascia which had been compressed and stained but not invaded. A portion of the frontal dura was in contact with the abnormal tissue, stained yellow but intact. The abnormal material was completely curetted away, and

the bony defect within the temporal fossa was covered with a small piece of tantalum.

The patient's recovery was uneventful and complete. The exophthalmos and diplopia disappeared rapidly.

### MICROSCOPIC PATHOLOGY

The findings are so similar in these four cases that a single description of the microscopic appearance seems justified. (Figs. 5 and 6.)

The most striking feature in all cases is a fibrous granulation tissue matrix containing clefts of the type correlated with cholesterol crystals. Numerous multinucleated foreign body giant cells are present along the periphery of many of the crystal clefts. The same elliptical spaces are seen in areas of complete tissue necrosis in which no cellular details can be stained.

In each case, there are other areas where few or no crystal clefts are seen in which there are large numbers of mononuclear cells arranged in broad sheets within a much more vascular stroma. Some of these cells have a large amount of strongly eosinophilic cytoplasm which sometimes contain particles of cellular débris and blood pigment. More often the same type of cell, usually a little larger and more spherical in shape, is seen with either a perfectly clear or vacuolated cytoplasm. Occasionally two nuclei are observed in these cells. Both the eosinophilic and foam cells are often present in clusters about blood vessels. Practically no necrosis is seen in these vascular areas, but in other regions where necrotic tissue is found one can usually identify the faint outlines of large foamy cells.

Small fragments of bone are scattered throughout the tissue and are frequently associated with multinucleated giant cells.

Yellowish-brown granules and crystals of various blood pigments are present in all regions, usually extracellularly, but sometimes as phagocytosed particles in the cytoplasm of the eosinophilic mononuclear cells or the foam cells. Scharlach-R fat stains demonstrate a large amount of neutral fat, some of which is within cells, but most of it lies free in the tissue. The contents of most of the foam cells are not stained by this method.

There are several small areas of dense infiltration by small inflammatory cells. Most of these are lymphocytes and polymorphonuclear leukocytes. Eosinophilic leukocytes are present in small numbers, both in these areas of infiltration and also scattered throughout the tissue in all except Case 1. These foci of small cells are usually but not always associated with areas of beginning necrosis.

Large amounts of fibrous connective tissue are found throughout the sections. Dense collagenous strands are usually most common at the periphery of the lesion. That portion of the tissue containing the multiple crystal clefts is also rich in fibrous tissue. The most delicate connective tissue pattern is visible in those areas of vascular stroma containing the larger mononuclear cells. Frequently delicate reticulin fibrils completely surround individual or small groups of foam cells.

Sections of bone taken from the margin of the lesions show infiltration of the adjacent marrow spaces by connective tissue containing both spindle and stellate types of cells. Increased numbers of round or oval cells are arranged in rows along the margin of bony trabeculae and are interpreted as osteoblasts. Neither eosinophilic mononuclear cells, foam cells or crystal clefts are found along the bony margins.

### SIMILAR CASES PREVIOUSLY REPORTED

Pincus[3] in 1933 described two very similar cases of unilateral exophthalmos due to localized destructive supraorbital lesions which were classified as "pseudo-cholesteatomas." The clinical, x-ray and gross pathologic findings in the two cases were practically identical; but since the microscopic material of one patient was lost, we have included only that case for which all data are available.

This was a forty-six year old man who had had pain, redness and tearing of the right eye for two years. There was no history of trauma. There was slight proptosis and downward displacement of the eye. X-rays showed a radiolucent area, about one-third the size of the orbital opening, in the lateral two-thirds of the right supraorbital ridge. The defect was fairly well demarcated from the surrounding bone. At operation a cavity was found within the bone from which some brown fluid escaped, and which contained yellow, soft, "porridge-like" material filled with crystals. Microscopic examination revealed no epithelial elements. There was no true capsule, only an irregularly

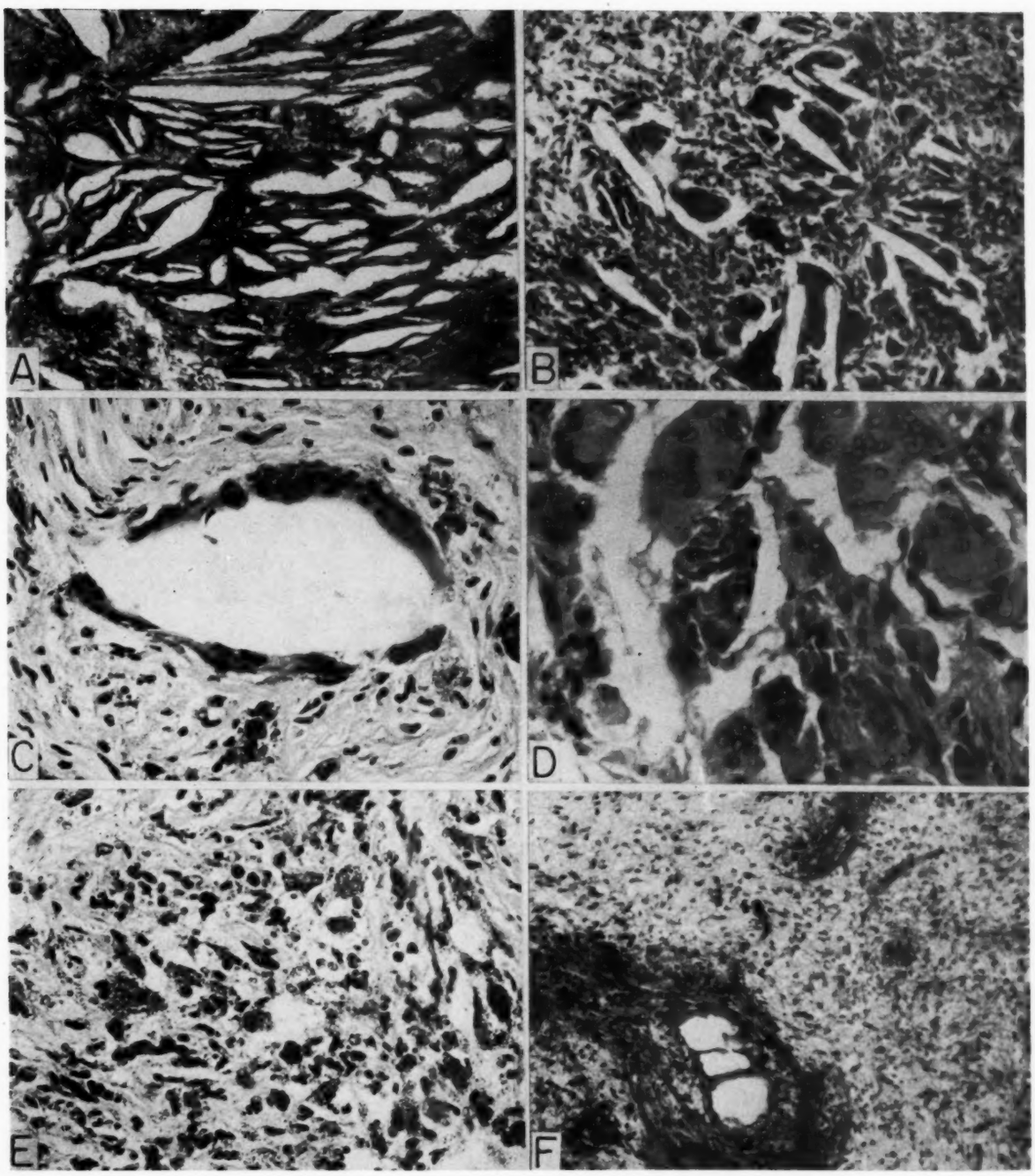


FIG. 5. A, (Case I) numerous cholesterol crystal clefts; phosphotungstic acid hematoxylin stain. B, (Case IV) crystal clefts surrounded by foreign body giant cells in granulation tissue matrix; cresyl-violet stain. C, (Case II) crystal cleft with surrounding foreign body giant cells; hematoxylin and eosin stain. D, (Case IV) numerous foreign body giant cells; hematoxylin and eosin stain. E, (Case II) blood pigment granules free in tissue and within histiocytes; hematoxylin and eosin stain. F, (Case IV) perivascular histiocytes and broad sheets of foam cells; hematoxylin and eosin stain.

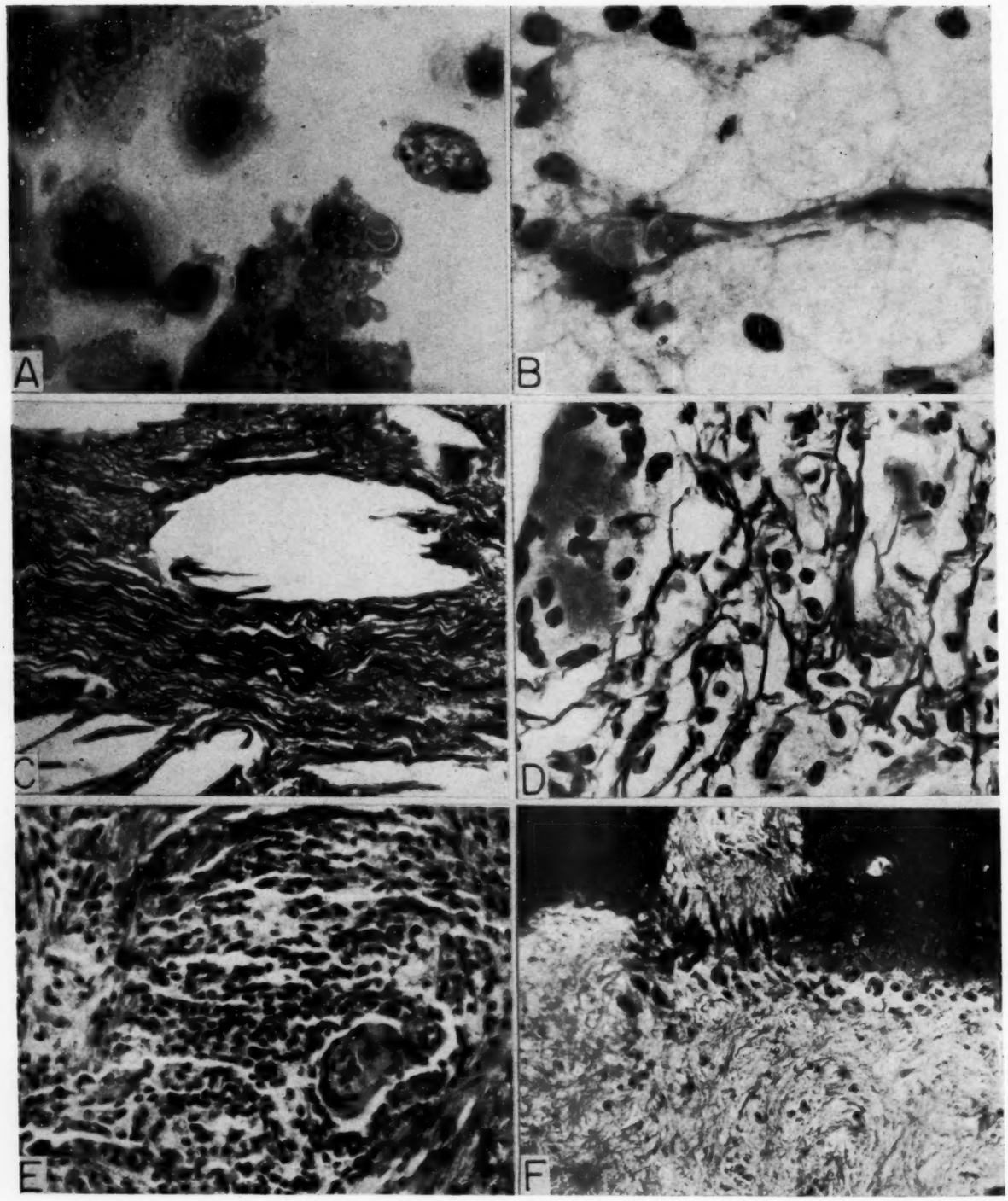


FIG. 6. A, (Case IV) histiocytes with eosinophilic cytoplasm displaying phagocytosis; hematoxylin and eosin stain. B, (Case III) foam (or xanthoma) cells with vacuolated cytoplasm; hematoxylin and eosin stain. C, (Case I) collagenous connective tissue in matrix containing crystal clefts; Laidlaw's connective tissue stain. D, (Case IV) reticulin fibrils among histiocytes and giant cells in the more vascular type of stroma containing no crystal clefts; Laidlaw's connective tissue stain. E, (Case IV) area of infiltration by inflammatory cells, predominantly lymphocytes; hematoxylin and eosin stain. F, (Case I) bony margin of lesion showing fibrous tissue which has invaded marrow space, and increased numbers of osteoblasts; phosphotungstic acid hematoxylin stain.

layered connective tissue structure. There were large numbers of extracellular cholesterol crystals either singly or in groups. Large numbers of foam cells and multinucleated giant cells were present. Various forms of blood pigment were seen throughout the tissue. Cultures of the material were sterile. The patient recovered well following surgery and had no symptoms during a three month follow-up.

Knapp[4] in 1934 reported two cases of unilateral exophthalmos due to expanding orbitofrontal lesions which he thought were examples of xanthomatosis of the orbit. The first case was a forty-three year old man who had had proptosis and failing vision of the left eye for three months. There was no history of trauma. A firm mass was palpable over the upper part of the left orbit. Visual acuity was reduced to 10/200. The blindspot was enlarged and a central scotoma was found. Examination of the fundus revealed optic neuritis, and the retina at the posterior pole had parallel folds. The eye was pushed forward and downward with restriction of upward motility. The right eye was normal. X-rays showed an osteolytic lesion in the upper and outer wall of the orbit not connected with the nasal sinuses. At operation the frontal bone overlying the lesion was found to be extremely thin. Beneath it there was a thickened soft membrane of a golden brown color. A cavity was opened which contained a thin watery fluid with many glistening yellow scales. Local curettage resulted in complete relief of symptoms. There was no clinical evidence of any other abnormality in other regions of the body. A single serum cholesterol value of 300 mg. per cent was found.

Knapp's second case was a twenty-eight year old man who had had proptosis of the right eye for two years. A firm mass was palpable within the upper border of the orbit which seemed to be continuous with the frontal bone. There was no history of trauma. An x-ray was not taken. At operation a thin bony wall was removed, exposing an irregular, lobulated, soft tumor within the upper wall of the orbit. An incision into this mass exposed a cavity filled with soft, gritty, "broken-down" material. The cavity extended deeply into the orbit, had eroded through the orbital roof and at one point was adherent to the dura. A seventeen year follow-up was available in this case. There had been no evidence of local recurrence or development of other similar lesions, and recent x-rays had shown only a small defect in the right upper orbital margin.

The microscopic appearance of both of these lesions was essentially the same. The main feature was the presence of numerous elongated crystal beds about which many foreign body giant cells had formed. Large numbers of lipoid-laden foam cells were found singly and in sheaths. Small cysts were occasionally present in areas where liquefaction was presumed to have occurred in regions of xanthoma or foam cells. Numerous small bony trabeculae were found surrounded by degenerating lipoid cells. There was no trace of epithelium in the tissue studied. Ewing studied this material and believed that the lesions were examples of xanthomatosis of the type observed in Schüller's disease.

Kreibig[5] in 1938 described a case of unilateral exophthalmos in a fifty-five year old man due to what he termed a "so-called cholesteatoma" of the supraorbital ridge. His patient had had a frontal sinusitis eleven years prior to the development of a painless proptosis of the left eye. There was no history of trauma. In addition to proptosis, the eye was displaced both downward and outward. The lateral two-thirds of the left supraorbital ridge was thickened and irregular but the overlying skin appeared normal. No abnormalities were found in the general examination. X-rays showed an osteolytic lesion with varyingly sharp and diffuse boundaries, containing soft calcifications, involving the supraorbital ridge from its mid-point to the zygomatic frontal suture as well as the roof of the orbit. At operation the periosteum was found to be raised from the frontal bone and the roof of the orbit and to have a brownish discoloration. The bone was eroded; and when the periosteum was torn a large amount of whitish or brownish "clumpy" material was released from the bony cavity. Microscopic sections showed masses of cholesterol mixed with varying amounts of blood pigment. Numerous cholesterol crystal clefts were present in granulation tissue with scattered foreign body giant cells. Foam cells, pigment-laden phagocytes, bone spicules and osteoclasts were seen. Collagenous connective tissue was present and was most dense about the periphery of the lesion. There was no evidence of any epithelial structure.

Ramsey et al.[2] in 1948 reported two cases of unilateral exophthalmos due to what they termed post-traumatic granuloma of the orbit. Their first case has been included in our present series (Case 1). Their second case was a forty-four year-old man who was first seen in February, 1947, complaining of prominence of the left eye and diplopia of seven months' duration. He had been struck over the left supraorbital region in 1912 and again in 1934, each time with no apparent sequelae. Examination disclosed a palpable swelling over the lateral portion of the left supraorbital ridge with proptosis and downward displacement of the globe. There was restriction of upward gaze with diplopia. Venous engorgement was observed in the left fundus. X-rays showed a concentric expanding lesion in the left frontal bone along the outer superior orbital margin which was thought to extend into the greater wing of the sphenoid bone. An operation was performed through the supraorbital region by Dr. H. Elliott on February 27, 1947. The frontal bone from the supraorbital notch laterally into the temporal fossa was bluish in color and extremely thin. When the "egg-shell-like" bone was opened, a cavity was found filled with a brownish, amorphous material. All the involved bone was removed together with the adjacent orbital fascia. Microscopic sections showed multiple elliptical crystal clefts and cholesterol crystals within a stroma of granulation tissue. Multinucleated giant cells and fat-laden phagocytes were scattered throughout the tissue. There was a large amount of different types of blood pigment both within phagocytic cells and lying free in the tissue. A great deal of collagenous connective tissue was present and was most dense about the periphery of the lesion.

## CLINICAL SUMMARY

*Age and Sex.* All of these nine cases occurred in males between the ages of twenty-eight and fifty-seven years. The average age was 43.3 years. Five of the nine patients were in the fifth decade. (Table 1.)

*History of Trauma.* Six patients denied having had trauma of any type to the orbitofrontal region. In three cases there was a definite history of trauma. Our Case III had sustained injuries on two occasions, one to the site of the lesion after symptoms had already been present, and another time in childhood in which a frontal laceration had been sustained on the opposite side. Two cases had very definite histories of trauma to the site of the lesion. In the second case reported by Ramsey et al. there had been two instances of trauma to the same region a matter of years prior to the appearance of symptoms. In our Case 1 there were also two episodes of trauma, but symptoms and signs of the lesions were already present at the time of the second accident.

*Duration of Symptoms.* Symptoms had been present for periods varying from a few weeks to several years. In our Case 1 a small painless swelling had been noted following trauma to the supraorbital ridge and had persisted for twenty-five years. A second accident involving the same region seemed to accelerate the growth of the lesion and led to his hospital admission.

*Symptoms.* Prominence of one eye and diplopia were the most common symptoms. Local pain, either referred to the eye or frontal region, was usually absent, being complained of by only two patients. Only one patient was aware of a supraorbital mass. Failing vision was recorded in only one instance.

*Signs.* All cases showed a unilateral exophthalmos which was usually not marked. In addition the globe was usually displaced inferiorly and medially. The only abnormality in extraocular movements was occasional restriction in upward gaze. Except for Knapp's two cases, visual acuity was found to be normal. The enlarged blind spot and central scotoma in Knapp's first case were the only abnormalities recorded in the visual fields of these nine cases. The pupils were normal in every case. Ramsey et al. noted retinal venous engorgement in one case, and Knapp recorded optic neuritis and parallel retinal folds in his Case 1. In all other instances opthalmoscopic examinations were negative. Six cases had some visible or palpable abnormality of the lateral portion of one supraorbital ridge. The nine cases were equally divided as to the side of the lesion, five being on the right and four on the left.

*Laboratory Data.* In no case was a significant abnormality recorded on examination of the peripheral blood. Anemia, marked leukocytosis, eosinophilia or elevated sedimentation rate were not encountered. Knapp's second case was the only one who had a positive blood Wassermann or Kahn reaction. In

those instances in which blood chemical studies were carried out no significant findings are recorded. Serum cholesterol levels were determined in only four cases. In Knapp's first case the level was 300 mg. per cent, which was considered evidence of a hypercholesteremia. The values we have recorded for three of our patients fell between the range of 150 to 250 mg. per cent, which is considered normal for the technic employed.

*X-ray Findings.* X-rays of the skull have been made on eight of the cases and are very similar. In each instance a rather well defined destructive lesion is present in the lateral portion of one supraorbital ridge. (Fig. 7.) The adjacent frontal squama and orbital roof have

TABLE 1

SUMMARY OF CLINICAL DATA IN NINE CASES OF CHOLESTEROL GRANULOMA OF THE ORBIT

| Author | Sex and Age | Trauma | Duration of Symptoms | Symptoms | Signs | X-ray Findings | Serum Cholesterol (mg. %) | Course after Local Excision |
|---|---|---|---|---|---|---|---|---|
| Pincus 1933 | M, 46 | No | 2 yr. | Pain, redness, and lacrimation of rt. eye | Proptosis and downward displacement of rt. eye | Osteolytic lesion in lateral portion of rt. supraorbital ridge | ... | Complete recovery; follow-up 3 mo. |
| Knapp 1934 | M, 43 | No | 3 mo. | Proptosis and failing vision of left eye | Reduced visual acuity, enlarged blind spot, central scotoma, and optic neuritis; eye displaced foreward and downward; upward gaze restricted; palpable tumor | Osteolytic lesion in upper and outer wall of left orbit | 300 | Marked improvement in vision; regression of proptosis; follow-up 9 mo. |
| Knapp 1934 | M, 28 | No | 2 yr. | Proptosis of rt. eye | Reduced visual acuity; forward and downward displacement of eye; palpable tumor | X-rays not taken | ... | Complete recovery; follow-up 17 yr. |
| Kreibig 1938 | M, 55 | No | 3 yr. | Proptosis of left eye | Eye displaced foreward, outward, and downward; thickened supraorbital ridge | Osteolytic lesion of lateral portion of left supraorbital ridge and roof of orbit | ... | Complete recovery; no follow-up |
| Ramsey et al. 1948 | M, 44 | Yes | 7 mo. | Proptosis of left eye and diplopia | Proptosis and downward displacement of eye; upward gaze restricted; retinal venous engorgement; palpable tumor | Osteolytic lesion in lateral portion of left supraorbital ridge, roof of orbit and greater wing of sphenoid bone | ... | Complete recovery; follow-up 7 yr. |
| Hanbery and Rayport 1954 | M, 57 | Yes | 25 yr. | Rt. supraorbital mass with recent enlargement and diplopia | Rt. eye displaced foreward, downward, and medially; palpable reddish swelling over lateral supraorbital ridge | Osteolytic lesion in lateral portion of right supraorbital ridge and roof of orbit | ... | Complete recovery; follow-up 3 yr. |
| Hanbery and Rayport 1954 | M, 31 | No | 18 mo. | Proptosis and pain in rt. eye; diplopia | Rt. eye displaced foreward, downward, and medially | Osteolytic lesion in lateral portion of right supraorbital ridge and roof of orbit | 195<br>178 | Complete recovery; follow-up 1 yr. |
| Hanbery and Rayport 1954 | M, 46 | Doubtful | 6 wk. | Proptosis of rt. eye and diplopia | Rt. eye displaced foreward and downward; upward gaze restricted; palpable tumor | Osteolytic lesion in lateral portion of right supraorbital ridge and roof of orbit | 222 | Complete recovery; no follow-up |
| Hanbery and Rayport 1954 | M, 40 | No | 2 wk. | Proptosis of left eye and diplopia | Left eye displaced foreward, downward and medially; diplopia on gaze upward and to the left | Osteolytic lesion in lateral portion of left supraorbital ridge and roof of orbit | 245 | Complete recovery; no follow-up |

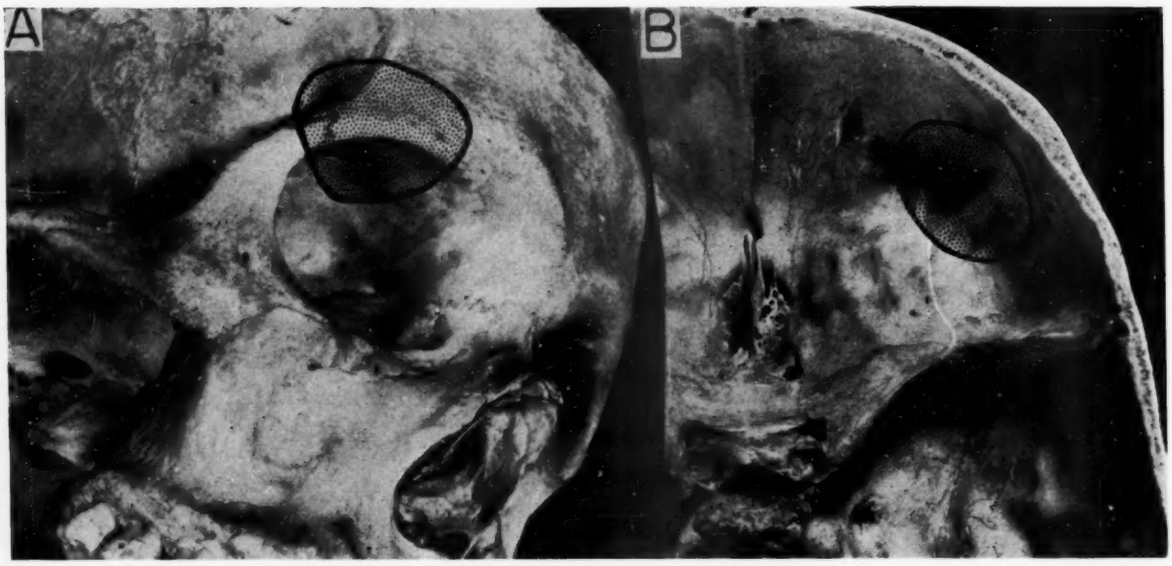


FIG. 7. The shaded area represents the usual extent of the osteolytic lesions involving the lateral portion of the supraorbital ridge, frontal squama, orbital roof, zygomatic process of the frontal bone, and that portion of the frontal bone just within the temporal fossa, as seen in A on the external surface of the skull and in B when viewed from above in the anterior fossa.

also been involved in varying degrees. In several lesions destruction is also apparent in the zygomatic process of the frontal bone. Although Ramsey et al. mention that the lesion in their Case 2 extended into the greater wing of the sphenoid bone, their x-ray evidence does not substantiate this statement. In all other cases the lesions were confined to the frontal bone and were separate from the frontal and ethmoid sinuses. The lesions have usually been partially separated by a thin line of compact bone from the normal diploic space. No other cranial or skeletal osteolytic lesions have been recorded.

*Treatment.* Each case has been operated upon and the abnormal tissue locally excised. Our Case II was the only patient in whom a craniotomy was performed with an extradural approach to the floor of the anterior fossa. All the other lesions were attacked directly either below or above the supraorbital border or through the temporal fossa. In each instance the abnormal tissue was curetted from the bony cavity. The orbital fascia was excised from Case 2 reported by Ramsey et al., but otherwise the removals were restricted to the granulomatous tissue and adjacent bone. Rather wide bony removals were carried out in the case of Ramsey et al. and in our Cases I and III. In the other cases only a minimal amount of bone was removed. While the dura has been found in contact with the lesion, there has been no intradural extension of the abnormal tissue. The roof of the orbit was found destroyed in varying extent in each case with compression of the orbital contents.

X-ray therapy had been given to only one patient (our Case II). There was a definite beneficial effect following the administration of 6,000 roentgens, but symptoms recurred after several months. Postoperative x-ray therapy was not employed in any of the cases.

*Results of Treatment.* All patients were rapidly relieved of their symptoms, and proptosis was corrected in each case. As far as is known recurrence has not been observed. Periods of observation have usually not extended beyond one year. However, our first case had no evidence of recurrence when last seen three years postoperatively. He is known to be alive now, ten years after operation, but it has not been possible to question or examine him. The second case reported by Ramsey et al. has recently been examined and x-rays have been obtained. He is asymptomatic and has no evidence of recurrence seven years postoperatively. Knapp recorded a remarkable seventeen year follow-up in one of his cases who had shown no signs of recurrence. What follow-up data are available in all cases have not revealed the presence of similar lesions in other parts of the body.

### PATHOLOGIC SUMMARY

*Gross.* The material contained within the cavity of the frontal bone was usually described as a soft, amorphous, gritty, golden or yellow-brown, avascular tissue. Descriptive terms such as "broken-down material," "mustard-like" and "grumous" were frequently used. Occasionally cystic fluid, either clear or "oily," in varying amounts was evacuated which sometimes contained obvious crystalline structures. Small amounts of old dark blood frequently escaped when the thinned bony wall was opened. A true capsule was never identified. No epithelial structures such as hair or white glistening tissue were ever found. The lesions all appeared to be well localized. The adjacent bone, while thinned in some areas, always seemed to have normal structure. While the orbital fascia and dura were frequently exposed and stained, abnormal tissue has not been found within the orbital capsule or within the dural membrane.

*Microscopic.* The most prominent histologic characteristic of all nine cases was the presence of multiple elliptical crystal clefts, often surrounded by foreign body giant cells, in a matrix of fibrous granulation tissue. Other constant findings were large numbers of foam or "xanthoma" cells, granules of blood pigment and varying amounts of collagenous connective tissue. In several cases, remnants of bony trabeculae were found, often associated with multinucleated giant cells. Mononucleated cells with eosinophilic cytoplasm, slightly smaller than the foam cells, were seen in our cases. Areas of infiltration by lymphocytes and polymorphonuclear leukocytes were occasionally observed. Scattered eosinophilic leukocytes were seen in three of our cases. Varying degrees of necrosis were recorded. All cases showed a connective tissue stroma which was usually most dense about the periphery and in the regions of accumulated crystal clefts. Delicate reticulin fibrils were frequently present among the foam cells. In no instance was any tissue found that might be interpreted as being of epithelial origin. In those cases in which adjacent bone was available for study, the only abnormality found was proliferation of connective tissue within the marginal marrow spaces and evidence of increased osteoblastic activity. A number of different pathologic diagnoses were made of these identical lesions: atypical cholesteatoma,[3,5] xanthomatosis of orbit[4] and post-traumatic granuloma.[2] Our first two cases were originally diagnosed as xanthomas.

### DIFFERENTIAL DIAGNOSIS

It is apparent that on clinical grounds alone one must include in the differential diagnosis almost all of the many causes of unilateral exophthalmos. From the roentgenographic point of view, the possibilities become somewhat restricted, but the findings reported for this lesion are not pathognomonic, and one must still consider such entities as neoplasm (benign or malignant), inflammation, fibrous dysplasia, osteitis fibrosa cystica, post-traumatic cyst, a form of lipidosis or any one of the types of histiocytic granuloma. The gross and microscopic pathology of such lesions therefore becomes paramount in establishing the proper diagnosis.

Considering together the clinical, radiologic and pathologic features of this group of cases, we believe that in the differential diagnosis one should consider (1) epidermoid and dermoid neoplasms, (2) giant cell tumor, (3) diploic hematoma, and (4) two of the types of what has recently been called histiocytic granuloma[6] or histiocytosis X,[7] namely, eosinophilic granuloma and Schüller-Christian's disease.

*Epidermoid and Dermoid Neoplasms.* From the clinical and roentgenographic point of view, it would not be possible to differentiate a diploic dermoid or epidermoid tumor from the lesion we have described in this report.

The presence of cholesterol crystals led Müller[11] in 1838 to suggest the term "cholesteatoma." However, it has since been shown that these crystals are neither an essential or constant finding on pathologic examination: many workers[8–10] believe that the term cholesteatoma is a poor choice and prefer to designate this type of growth as an epidermoid. Epidermoid and dermoid tumors are now considered to be of congenital origin, occurring as the result of a fetal inclusion of epidermal cells. Depending on the depth of the epidermal layer, or according to the embryonic age, either an epidermoid or a dermoid type of tumor is produced.

The gross appearance of the epidermoid tumors is often striking, the glistening white capsule immediately suggesting the pearl-like sheen originally described by Cruveilhier[12] in

1829. Since this same appearance has been found in a few dermoid tumors, it cannot be accepted as pathognomonic. Fragmentation, caseation and necrosis may be observed within the epidermoid lesions. When the tumors are sectioned, they frequently show a uniform consistency of a finely granular, avascular, white or creamy yellow, laminated material with a soapy or waxy quality. Microscopic examination usually reveals some form of epithelial structure, keratin, keratohyalin, collagenous connective tissue and products of desquamation, including cholesterol crystals.

Dermoid tumors are usually soft, cystic and have an opaque yellow color, although they may infrequently have a pearly sheen. Fat, sebaceous material, cholesterol crystals and hairs in various forms are usually observed within the neoplasm. Histologically, these lesions contain structures of both epithelium and corium, with epithelial cells, sebaceous glands, hair follicles, fat cells, smooth muscles, elastic fibers and blood vessels. Calcification with bony or cartilagenous spicules may be found in the connective tissue matrix.

It is apparent that on pathologic grounds the lesions we are discussing are neither epidermoid nor dermoid neoplasms of the orbit.[13,14] Both Pincus and Kreibig failed to find any trace of an epithelial structure in their cases and hesitated to call them true cholesteatomas of the orbit. Since they were unable to offer another diagnosis and because of the high cholesterol content of the pathologic tissue, they suggested the ambiguous terms "pseudocholesteatoma" and "so-called cholesteatoma." Knapp reviewed the cases reported by Pincus and was of the opinion that the lesions were identical with those he described as examples of xanthomatosis of the orbit.

*Giant Cell Tumor.* Giant cell tumors of the skull are rare lesions which are stated to occur only in those bones which develop from the chondrocranium. This was true of the four cranial neoplasms reported by Geschickter and Copeland[15] in their series of over 300 skeletal and extraskeletal giant cell tumors. They cite one case reported by Fraser[16] as occurring in a membranous bone of the skull. This lesion of the frontal bone was removed and on section showed blood spaces surrounded by giant cells. Geschickter and Copeland[15] suggest that it was not a giant cell tumor but a post-traumatic vascular defect with giant cell osteoclasts. It should be noted that all nine of the cases reviewed in the present report involved the frontal bone, which is of membranous origin.

Three of the microscopic elements of the orbitofrontal lesions under discussion—giant cells, xanthoma or foam cells, and pigment-laden phagocytes—are seen in xanthomatous variants[17] of the giant cell tumors, but this type of neoplasm has been extraskeletal in location and never observed in the skull.

The matrix of the giant cell tumors is entirely different from that seen in the granulomatous lesions under discussion, and the large amount of extracellular cholesterol has not been observed. On histologic grounds alone it is apparent that we are not dealing with giant cell tumor of bone or any of its variants. Chorobski and Davis[18] collected together the few rare cases of cranial bone cysts affecting the membranous bones thought to be due to osteitis fibrosa cystica accompanied by areas simulating giant cell tumor. The pathologic material they present does not resemble that seen in our cases. Geschickter and Copeland[19] reviewed approximately 200 cases of solitary bone cysts, and found none involving the membranous bones of the skull.

*Diploic Hematoma.* In only two of the nine cases was there a definite history of trauma to the site of the lesion which antedated all signs and symptoms. These were the two cases reported by Ramsey et al.[2] (including our Case 1). In our third case there had been minimal trauma to the involved supraorbital region after unilateral exophthalmos had already been recognized, and the indefinite history of craniofacial injury sustained in childhood may or may not have been significant. In all the other six cases no history of trauma could be obtained. It must be admitted, however, that minimal trauma to the orbitofrontal region, especially the outer one-third of the supraorbital ridge, must be extremely common and might be overlooked when sought for months or years later. The fact that all cases occurred in young and middle-aged males might also emphasize the etiologic significance of trauma.

Ramsey et al. considered trauma to be the initiating factor in their cases with the production of a diploic hematoma. They did not believe it was necessary for fracturing to occur. They suggested that the sterile decomposition products of blood, such as pigment and

cholesterol crystals, provoke a foreign body granuloma. This leads to a slowly progressive expanding diploic lesion which erodes both cortices of the orbitofrontal bone by pressure, finally breaking through the thin orbital roof to cause unilateral exophthalmos. These authors believed that the essential lesion was a chronic granuloma composed of granulation tissue about multiple elliptical cholesterol crystals, with foreign body giant cells, fat laden phagocytes (foam cells), various blood pigments and fibrous connective tissue. To them, this lesion was the same as that observed in granulomas of soft tissues following hemorrhages, injury to body fat, injection of hydrolyzable oils into the tissues, and when the cholesterol and fatty acid contents of epithelial cysts had been extravasated into the surrounding tissues.

This single theory is attractive, and when only those cases reported by Ramsey et al. are considered, seems plausible. However, after reviewing additional material, it seems to us that there are certain objections to such an explanation. Craniofacial trauma is very common; these lesions are rare. The granulomatous lesions appear identical in those few cases in which trauma has seemed significant and in the larger number who give no history of trauma.

*Histiocytic Granuloma.* The final point to be considered in the differential diagnosis is the pathologic process which we have chosen to designate, with Goodhill,[6] as histiocytic granuloma. The present concept of this disease entity has been reached after a long and devious route characterized by confusion in terminology and interpretation.

Between 1893 and 1928, twelve scattered cases[20] were reported of children with defects in the membranous bones, exophthalmos and diabetes insipidus. Such cases came to be referred to as Hand-Schüller-Christian's disease, Schüller-Christian's disease or Christian's syndrome. There was no clear understanding of the basic pathologic process. Rowland[21] in 1928 reviewed these twelve cases, added two of his own and concluded that the lesions were granulomatous and not neoplastic. In his opinion the basic abnormality was a disturbance of lipoid metabolism with an excess of this substance in the body fluids. The resulting diffuse or nodular hyperplasia of the reticuloendothelial cells was an attempt to store and rid the body fluids of the particular lipoid substance whose normal excretion had become impaired. He spoke of "lipoid gout" and compared the abnormalities of lipoid and uric acid metabolism. Rowland concluded that all of the previously described xanthomatous lesions, such as those affecting the eyelids, tendon sheaths, and the more generalized skin eruptions, were all examples of a disturbed cholesterol metabolism. He, likewise, was of the opinion that Schüller-Christian's disease was another form of xanthoma ("generalized visceral xanthoma-xanthomatosis"), was also based on faulty cholesterol metabolism, and that it was related to other types of lipoid storage diseases such as Niemann-Pick's and Gaucher's disease. He proposed the general term xanthomatosis to include all of the various types of lipoid storage lesions which might involve the reticuloendothelial system. For him, the fact that the granulomatous lesions of Schüller-Christian's disease were sometimes solitary did not necessarily separate them from the generalized group but indicated that there might be secondary factors, such as trauma, irritation or infection which determined their localization.

Soon other workers began to designate Schüller-Christian's disease by different terms, such as lipoid granuloma,[22] skeletal lipoid granulomatosis,[23] xanthomatosis,[24–28] chronic idiopathic lipoidosis,[29] metabolic histiocytosis[30] and essential xanthomatosis of the normal cholesteremic type.[31] The most commonly used term was probably xanthomatosis which came to be considered as a synonym for Schüller-Christian's disease, thereby losing Rowland's original meaning as a general term for all types of lipoid storage disease. As more cases were studied, it gradually became apparent that the majority of patients did not have an elevated blood serum cholesterol, and considerable doubt was cast on the theory that Schüller-Christian's disease was based on an abnormal lipoid metabolism with a hypercholesteremia. Most pathologists therefore believed that this disease should not be considered one of the lipoidoses and included in the latter group only Niemann-Pick's disease, Gaucher's disease, Tay-Sach's disease and those xanthomatous lesions (such as xanthoma tuberosum multiplex) that are associated with a hypercholesteremia.

During the past fifteen years many workers[6,7,32–43] have come to believe that Schüller-Christian's disease is closely related to Letterer-

Siwe's disease and eosinophilic granuloma of bone, some postulating that they each represent merely a phase of the same disease process. Several terms have been suggested for this pathologic entity, such as eosinophilic xanthomatous granuloma,[32] reticuloendothelial granulomatosis,[33] inflammatory histiocytosis,[30,34] reticuloendotheliosis,[35–37] reticulogranuloma[38–40] and histiocytic granuloma.[6] Lichtenstein[7] has recently reviewed this entire subject. He believes that none of the proposed terms are completely satisfactory and has suggested the name "histiocytosis X" as a provisional general designation for this nosologic entity. While trauma and various types of infection have been suggested as possible etiologic factors, no direct evidence has been presented, and the disease is considered to be a granulomatous lesion of unknown origin involving the tissue histiocytes or the reticuloendothelial system.

Even though most would agree that these three diseases are closely allied and that both clinical and pathologic features of one may merge into the other, definite proof has not yet been presented that they represent an acute, subacute and chronic form of exactly the same disease process. Because certain of the clinical and pathologic features of these three lesions retain a characteristic pattern, they will probably continue to be referred to by those names which are so firmly established in medical literature. It may perhaps be worth while to refer to them collectively as the histiocytic granulomas of Letterer-Siwe, eosinophilic granuloma and Schüller-Christian types.

1. *Letterer-Siwe's disease* (aleukemic reticuloses, diffuse reticuloendotheliosis, non-lipoid histiocytosis): This is usually a rapidly fatal illness of infants or children characterized by lymphadenopathy, splenohepatomegaly, cutaneous petechiae, bone defects, hypochromic anemia and fever. The bone defects are usually multiple and by x-ray appear the same as those in the other two types of disease. Microscopically, the diffuse visceral and skeletal lesions are characterized by dense proliferation of large histiocytes which usually do not contain lipoids. Multinucleated giant cells are present and occasionally eosinophilic leukocytes can be seen. There are no extracellular cholesterol crystals. From both clinical and pathologic viewpoints the present lesions cannot be considered a part of Letterer-Siwe's disease.

2. *Eosinophilic granuloma of bone* (solitary[44] or destructive[45] granuloma of bone): These lesions are usually found in children, adolescents or young adults. Very often only one bone is involved; in others, however, there may be multiple skeletal lesions. The skull is frequently involved, especially the frontal bones. In about one-quarter of the cases trauma to the same site is said to have antedated signs or symptoms. Sometimes there is slight swelling and tenderness over the lesion. The general health of the patient remains good. There may be a mild leukocytosis and in a few instances an eosinophilia is noted. The x-ray appearance of the bony defects is not characteristic. The pathologic material has been described grossly as soft, cellular tissue, yellow-brown, gray-white or gray-pink in color. Microscopically, the lesions are composed of histiocytes whose cytoplasm may contain cellular débris and blood pigment but is usually free of lipoid. There are scattered multinucleated giant cells, and varying numbers of eosinophilic polymorphonuclear leukocytes. No extracellular cholesterol crystals are present, and there is very little fibrous connective tissue.

Prognosis is considered good in cases of eosinophilic granuloma, the lesions usually healing following curettage, x-ray therapy or even spontaneously.

Wheeler[46] described a case of unilateral exophthalmos in a thirty-four year old man caused by an orbitofrontal eosinophilic granuloma. X-rays showed a destructive lesion in the frontal bone above the lateral one-half of the supraorbital ridge and extending into the lateral portion of the orbital roof. This appeared as an osteolytic lesion surrounded by a thin layer of compact bone, and resembled exactly the skull defects observed in our own cases. The gross and microscopic descriptions were typically those of eosinophilic granuloma.

Many clinical and x-ray features of our cases would be compatible with the diagnosis of eosinophilic granuloma of bone, but the age range is usually lower and the histologic finding of cholesterol crystals and fibrosis precludes this diagnosis.

3. *Schüller-Christian's disease* (xanthomatosis, lipoid histiocytosis,[47] lipoid granuloma, lipogranulomatosis): This is usually considered to be predominantly a disease of children with

widespread visceral and skeletal lesions of a lipogranulomatous nature. The classical triad of Christian's syndrome may be partially or completely present, or may be entirely lacking. The disease may also occur in adults, even as late as the fifth or sixth decade. Cases with only solitary lesions have been reported. It has been suggested that some of them may have originally existed as eosinophilic granulomas, but this has not been proven.

Both visceral and skeletal lesions have been shown by several workers to have the same microscopic features. Large numbers of lipoid-laden histiocytes (xanthoma or foam cells) are arranged either about vessels or loosely within a vascularized connective tissue stroma. Granules of various types of blood pigment are also present lying free or within the cytoplasm of the foam cells. Sometimes the fatty substance is extracellular occurring as fine crystals united in clusters and surrounded by numerous foreign body giant cells. Occasional areas are infiltrated by varying numbers of lymphocytes, plasma cells, polymorphonuclear leukocytes and eosinophils. In the early development of the lesions xanthoma cells in a vascular stroma of granulation tissue is the striking feature; while in the older lesions various stages of fatty degeneration, foreign body reaction and fibrosis occur.

It is generally agreed that hypercholesteremia is not a prerequisite. In those few cases in which the serum cholesterol has been found above the normal range of 150 to 250 mg. per cent, it has been suggested that the elevation may be due to a transient mobilization of cholesterol which is present in the granulomatous lesions in amounts up to twenty times that found in normal tissue.

The two cases reported by Knapp in 1934 as instances of xanthomatosis of the orbit would seem to be identical with those of Ramsey et al., Pincus, Kreibig and our own. There was no history of trauma in either of his cases. In the one case in which blood chemistry studies were done, a hypercholesteremia of 300 mg. per cent was found. Both Knapp and Ewing, who reviewed the pathologic specimens, believed that the lesions were granulomatous, not neoplastic, and that they were entirely different from cholesteatomas of epidermal origin. They visualized the destructive lesion as originating within the bone marrow with an accumulation of xanthoma cells due to an excess storage of lipoids, with later degeneration into cystic spaces and extracellular clusters of cholesterol crystals with a resulting foreign body giant cell and connective tissue reaction. The extremely long follow-up on one of the cases with no evidence of local recurrence following local excision or development of other similar lesions led Knapp to believe he was dealing with a benign disease.

Dandy[48] in 1941 described thirty-one cases of orbital tumor and included in this group five cases of what he thought was probably Schüller-Christian's disease. His first case was a forty-six year old man who had noted slight swelling of the left upper eyelid for two and one-half months. He had a slight amount of exophthalmos of the left eye with a slight swelling and palpable bony defect in the lateral portion of the left frontal bone involving the orbital roof. The abnormal tissue was described as grayish-white, grossly cellular and unencapsulated. It was adherent to the exposed orbital capsule and to the dura mater. The lesion was widely excised, and the patient was entirely well when last contacted seven months postoperatively. Dr. Arnold Rich described the microscopic aspects of the lesion as being "like that found in the marrow in Schüller-Christian's disease." There were many mononuclear macrophages, foam cells and eosinophils. In some areas there was dense hyalinized connective tissue with foci of small mononuclear cells, particularly about the blood vessels. No mention was made of giant cells or cholesterol crystals. With the exception of these two points, his case entirely resembles those we have described.

The other four cases were quite different. In none of these was a skull defect demonstrable. Microscopic examination disclosed them to be non-neoplastic lesions which Rich and Dandy believed resembled Schüller-Christian's disease more than any other entity. The pathologic material presented for each of the cases was extremely meager, and it is difficult to evaluate this aspect of the lesions.

### CONCLUSIONS REGARDING NATURE OF LESION

After reviewing the various aspects of our own four cases, the five similar ones previously reported, and the pertinent literature, we have formed certain opinions regarding the pathologic aspects of these orbitofrontal lesions. We do not believe they are epidermoid or dermoid neoplasms, or giant cell tumors. Trauma alone

with the production of a diploic hematoma appears inadequate to explain the pathogenesis of all of these lesions. Evidence is lacking that infection, either secondary to paranasal sinus disease or metastatic on the basis of a bacteremia, is an important etiologic factor. Since it has been shown that there is no basic disturbance of cholesterol metabolism, the term xanthomatosis should be eliminated in relation to this disease process.

We are unable to explain the etiology of these lesions and are of the opinion that, for the present at least, a purely descriptive terminology is most useful. Since large numbers of cholesterol crystal clefts have been the most striking microscopic pathologic feature, we have suggested the term cholesterol granuloma.

One might speculate that these lesions represent a chronic, benign form of the histiocytic granulomas of the Schüller-Christian type, occurring in adults as a solitary destructive lesion of bone, with a tendency to be localized in the lateral orbitofrontal region and to produce varying signs and symptoms of unilateral orbital compression. It would seem possible, though as yet unproved, that such lesions might originally have been eosinophilic granulomas of bone, which gradually underwent fatty degeneration and developed a marked ingrowth of fibrous connective tissue. If so, this would relate the case of Wheeler and the first case of Dandy's series to the nine cases we have reviewed. Wheeler's case was both clinically and radiologically the same as ours, but showed a typical eosinophilic granuloma in a young man. Dandy's case, also identical to ours in clinical and x-ray findings, might have represented an intermediate lesion with foam cells and fibrosis, but with no cholesterol crystals or giant cells. Finally our cases, all of which contained lipoid material and collagenous connective tissue with few eosinophils, might represent the most chronic form of the granulomatous lesion.

However one chooses to catalogue these destructive lesions of bone, certain aspects of their structure and behavior now seem clear, which are of practical importance in the case of the individual patient. The pathologic process is that of a granuloma and not a neoplasm. It is not one of the lipidoses based on faulty cholesterol metabolism. When it is observed as a solitary lesion in an adult, there is little likelihood that other skeletal or visceral lesions will develop. Adequate local excision will lead to rapid and permanent relief of symptoms.

### TREATMENT

Therapy can be planned only after the diagnosis has been established, and since the clinical and x-ray findings are not pathognomonic, most cases will be operated upon to ascertain the pathologic nature of the lesion. There would seem to be little reason to perform a needle biopsy, since excision is probably the treatment of choice. It is true that x-ray therapy has proven of value in cases of eosinophilic granuloma, Schüller-Christian's disease, and even diploic hematoma. Case II in our series was temporarily improved after x-ray therapy, but his symptoms recurred after several months. The characteristic gross appearance of the lesions, easily confirmed by rapidly stained smears and frozen sections, allows definitive therapy to be carried out at the time the lesion is first visualized.

The operative approach has varied depending on the size and location of the lesion and whether the operation has been performed by an ophthalmologist or a neurosurgeon. Ophthalmologists have occasionally used a lateral canthotomy, not always with adequate exposure. Other of these lesions have been approached through incisions just below, through or above the eyebrow. Dandy[48] and Reichert (Case 2) have employed a transfrontal approach. In our Cases I and III a curved frontal incision was made and the scalp flap reflected anteriorly. A bone flap was not turned, however, and the bony lesion was attacked directly.

It seems to us that most of these lesions can be treated through an anterior approach and should not require craniotomy. If the lesion extends laterally and presents within the temporal fossa just posterior to the zygomatic process of the frontal bone, a modified Krönlein approach offers certain advantages. With an incision through the lateral one-half of the eyebrow extending slightly along the zygomatic process, the anterior most portion of the temporal fascia and muscle can be mobilized and retracted posteriorly, exposing the eroded portion of the frontal bone. The cavity can easily be broken into in this location, a biopsy obtained and curettage completed, without destroying what remains of the supraorbital

ridge. Even though the frontal squama is greatly thinned, any covering of bone which remains, together with the periosteum, should be preserved. Those cases involving only the frontal squama and orbital roof can be adequately approached through a brow incision, entering the cavity through the orbital roof and preserving the supraorbital ridge and frontal squama.

Those cases with extension backward to involve the posterior portion of the orbital roof can perhaps be visualized better through the transfrontal approach as advocated by Dandy. This is especially true for any case in which there is either clinical or x-ray evidence of more than minimal intraorbital extension.

Whatever approach is used, it is apparently only necessary to remove the soft, yellowish-brown, amorphous, gritty material completely by curettage. It is not necessary to remove the adjacent bone radically; in fact, an attempt should be made to preserve whatever remains of the supraorbital ridge and frontal squama. Orbital periosteum, frontal pericranium, orbital fascia and dura which are in contact with the abnormal tissue need not be sacrificed. Care should be taken to avoid entering the paranasal sinuses as well as lacerating the dura and producing a cerebrospinal fluid fistula. If a conservative removal is performed, the bony cavity will usually fill in with regenerated bone and cranioplasty will probably not be necessary.


## SUMMARY

1. The clinical and pathologic features of nine cases of orbitofrontal cholesterol granuloma have been summarized.

2. All lesions were solitary and occurred in young or middle-aged adult males.

3. There was a definite history of trauma in two cases.

4. Unilateral exophthalmos and diplopia were the most common symptoms.

5. Forward, inferior and medial displacement of the eye with restriction of upward gaze were the most constant findings. In six cases there was a visible or palpable abnormality of the lateral portion of one supraorbital ridge.

6. There was radiographic evidence of an osteolytic lesion in the lateral portion of one supraorbital ridge with involvement of the adjacent frontal squama, orbital roof and zygomatic process of the frontal bone in all eight cases in which x-rays were taken.

7. All patients were operated upon, disclosing a cavity in the bone filled with a soft, yellowish-brown, amorphous, gritty substance. There was compression of the orbital fascia in each instance. No invasion was demonstrated through the orbital fascia or frontal dura.

8. The microscopic appearance in all cases was that of a granuloma containing large numbers of cholesterol crystal clefts, foreign body giant cells, foam cells, histiocytes with eosinophilic cytoplasm, inflammatory cells, blood pigment and collagenous connective tissue.

9. Local excision has resulted in prompt recovery and there has been no evidence of recurrence. A conservative operative approach and curettage has been recommended.

10. The etiology and pathogenesis remain unknown. It is suggested that these lesions may be related to the histiocytic granulomas of the Schüller-Christian type, but conclusive proof is lacking.


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# Surgical Treatment of Rheumatic Tenosynovitis

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NON-SPECIFIC tenosynovitis has been recognized for many years but should be brought to attention anew because of existing confusion as to etiology and its relationship to industrial injury.

Tenosynovitis is the response of a tendon sheath to irritation. The cause of the irritation may be specific, such as bacterial invasion or trauma of some kind. The disease may be acute or chronic. When the exact cause of the irritation is not evident, even after bacteriologic and pathologic study, the term "nonspecific tenosynovitis" is generally used. Cases of this classification are chronic in nature and resistant to the usual forms of conservative therapy. Remissions and exacerbations are common, and in all such cases symptoms become more pronounced when the involved tendons are activated as in work.

That this form of tenosynovitis is a rheumatic disorder and therefore a manifestation of a systemic disease seems highly probable in the light of existing information.

## REVIEW OF THE LITERATURE

Vischer[12] reported on seven cases, all previously diagnosed as tuberculosis. Positive evidence of tuberculosis could not be found in a careful study, but in all cases rheumatic nodules were present in material microscopically examined. An analogy was drawn between these nodules and the Ashoff bodies found in acute rheumatic fever.

Kanavel[7] reported on fourteen cases of tuberculous tenosynovitis of the hand. However, in only one case was there associated pulmonary tuberculosis; in the remainder there was no evidence of tuberculosis elsewhere. It was not stated whether or not tubercle bacilli were found locally. Cordes[4] likewise was unable to identify the tubercle bacillus in this disease and he expressed the opinion that the condition is related to rheumatism.

Albertini[1] used the term "fungose" to describe this form of tenosynovitis. He stated the condition is non-tuberculous but did not agree with Vischer and Cordes that the disease is rheumatic.

Günther[6] used the term "hygromatous rheumatica" in a discussion of the problem and remarked that fluid may or may not be present in the involved tendon sheath. He also commented that although the histologic features resembled those of tuberculosis, the tubercle bacillus was not found in smear or animal inoculation in any of the reviewed cases.

Klinge,[10] reporting a careful histologic study, said that the microscopic appearance of the involved tendon sheath is practically identical with the changes noted in polyarthritis. He was unable to find any evidence of tuberculosis.

Continuing the work of Kanavel, Mason[11] reported thirty-three cases of chronic tenosynovitis of the hand and said that in twenty-three there was histologic proof of tuberculosis; but here again no mention was made of whether or not the tubercle bacillus was isolated. Six of the entire series of cases were classed as rheumatic tenosynovitis, with the mention that these cases were hardly distinguishable from the others which were termed tuberculous.

Edström,[5] reporting upon examination of all chronic rheumatic patients for the year 1943 at the Lund Hospital in Sweden, said that 48 per cent showed tendinous involvement, and in 42 per cent there was upper extremity involvement. The most common location of the tendon involvement was the flexors of the fingers (35 per cent), and Edström ventured to say that such involvement may be the first symptom of polyarthritis.

In a report of two cases of tenosynovitis in patients with chronic polyarthritis. Baumgartner[2] noted the presence of rheumatic

nodules in the microscopic study of the involved tendon sheath.

Kellgren and Ball[8] noted that tendon lesions were present in forty-two of 100 cases of rheumatism. Pathologic description was made from material obtained by thirty-eight biopsies of tendinous lesions. The essential features were local fibrinoid degeneration followed by granulation tissue.

Six cases of tumorous lesions on the dorsum of the hand were reported by Kestler.[9] One was proved to be tuberculous. In the other five a diagnosis of rheumatoid disease was made pathologically. In two of the five cases rheumatoid arthritis developed later. Although the description closely fitted that of rheumatic tenosynovitis, Kestler considered the five cases a new entity, which he named collagenous pseudotumors of tendon sheaths.

Bickel, Kimbrough and Dahlin[3] remarked on the rarity of tuberculous involvement of tendon sheaths. They reported on fifty-two cases observed at the Mayo Clinic between the years 1915 and 1949 in which tuberculous involvement of tendon sheaths was diagnosed—proved by bacteriologic and histologic examination in thirty-seven cases.

The present study is based on eleven cases, from a group of cases of so-called non-specific tenosynovitis, selected as representative on the basis of similarity of complaints, physical findings and conditions observed at operation.

Of the eleven patients, five were women and six were men. As three of the patients, a man and two women, had bilateral disease, the total number of operations was fourteen. The average age of the women was forty-one years and that of the men forty-four years. The youngest patient in the series was a man twenty-three years of age and the oldest a man aged fifty-eight. The average duration of symptoms in the women was 2.4 years; in the men, 2.6 years. In the three cases of shortest duration of symptoms—one month in two cases and two months in another—the patients were men and industrial injury was claimed as the cause. The longest duration of symptoms, fourteen years, was also in a man.

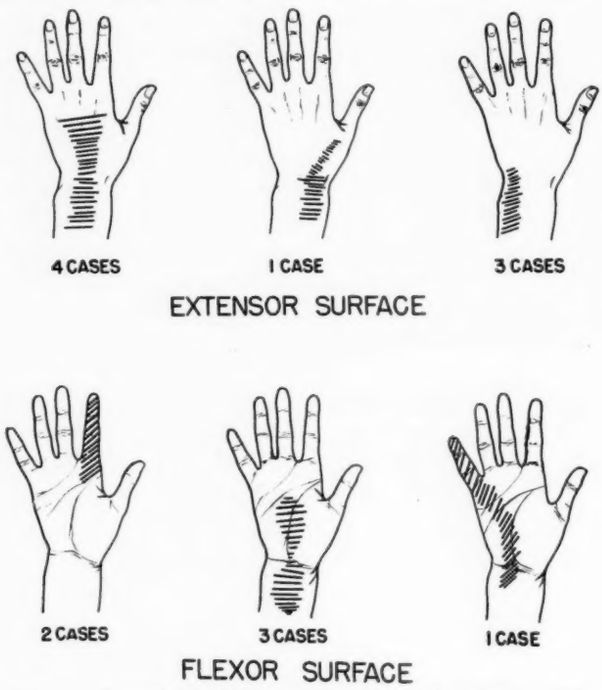
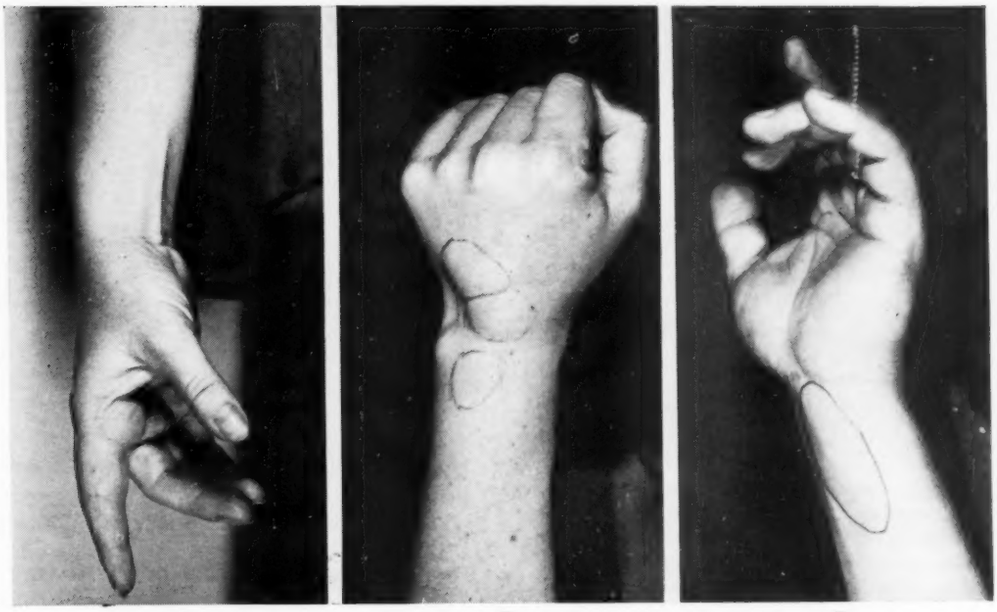



FIG. 1. Location of fourteen areas of involvement in eleven cases.

Six of the eleven patients had involvement of the extensor surface, four had involvement on the flexor surface and one had involvement on both extensor and flexor surfaces. The specific locations of the fourteen areas of involvement (Fig 1) were as follows: Flexor surface, two involving the sheath of the long flexor tendon of the index finger, three in which the digital flexors were involved in the distal forearm and palm, and one in which the entire ulnar bursa



2A 2B 2C

FIG. 2. A, rheumatic tenosynovitis of digital flexor tendon sheath of index finger. Note general swelling of the finger and bulge of cul-de-sac in distal palm. B, rheumatic tenosynovitis of extensor digitorum communis sheath at wrist level, both distal and proximal to transverse dorsal carpal ligament. The contained fluid could be pressed to either side of the ligament. C, an extensive case of rheumatic tenosynovitis involving the digital flexor tendon sheaths in the palm and above the wrist. Note the abnormal stance of the index and little fingers due to direct tendon damage by the process.

was involved; extensor group, four cases of involvement of the extensor communis tendons of the fingers at the wrist level; three cases of extensor carpi ulnaris involvement, with additional involvement in two of the three, consisting in one instance of involvement of the sheath of the extensor digiti quinti proprius, the head of the ulna and the distal radioulnar joint, and in the other instance involvement of the styloid process of the ulna and the wrist joint. In the remaining case there was involvement of the extensor carpi radialis tendons and of the long extensor tendon of the thumb at wrist level.

In all cases there was complaint of swelling at the time of first examination. The other symptoms in the order of their frequency were as follows: pain, limited motion, crepitus and weakness. Of particular significance was the fact that in eight of the eleven cases there was a history of previous rheumatic joint disease or of tenosynovitis of a similar type; and in two cases typical rheumatic joint involvement was noted to be in progress during the period the tenosynovitis was being treated. In only two cases was there previous history of tuberculosis. Both patients were women, one with a history of minor pulmonary involvement at the age of eighteen years and the other with a history of suppurative cervical adenitis at the age of ten years. Active disease was not present in either case at this time.

The diagnosis is based primarily on the history and the presence of a boggy swelling, involving one or more tendon sheaths. (Fig. 2.) Often if pressure is applied to one area of the sheath, swelling increases at the opposite end owing to a change in location of the fluid. A crepitant sensation may also be present if granulation tissue or rice bodies are abundant. The skin is seldom if ever involved. There are no signs of acute inflammation, either local or systemic. A history of previous rheumatic joint disease or of other stigmas of rheumatic affliction is most likely. Stiffness of a joint may be noted, or active disease within the joint may be present. The presence of knuckle "pads" or palmar fascia thickening may give additional evidence of a general rheumatic diathesis. The differential diagnosis could include such entities as ganglion or tumor of the tendon sheath; however, the principal one is tuberculous tenosynovitis, which can so closely resemble rheumatic tenosynovitis clinically

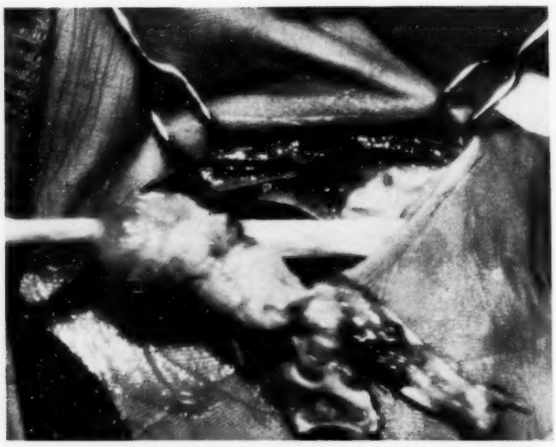


FIG. 3. Operative field in distal palm at base of index finger showing removed sublimis tendon and flexor tendon sheath in foreground. Note polypoid granulation tissue filling the sheath and attached to the tendon, which in some areas was actually invaded. The profundus flexor tendon trimmed smooth of granulation tissue may be seen in the background.

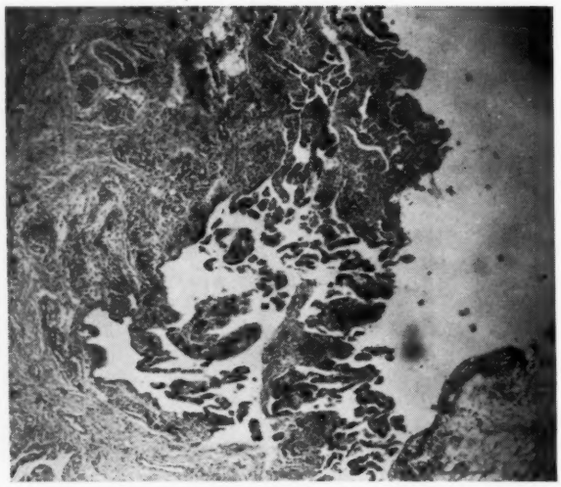


FIG. 4. Low power microscopic view of tendon sheath showing marked polypoid proliferation of lining.

that only by careful study and detailed examination of the removed tissue can the distinction be made.

### SURGICAL TREATMENT AND OPERATIVE FINDINGS

In the present series surgical treatment at each involved site consisted of complete, meticulous excision of the tendon sheath. Good visibility of the operative field was brought about by using a tourniquet for ischemia. In each instance the swelling present was due to distention of the involved sheath by clear, straw-colored fluid and an abundance of granulation-like tissue having a polypoid or villous form. (Fig. 3.) The sheath structures were thickened. In seven instances there was direct involvement of the tendon consisting of an ingrowth of granulation tissue into the tendon with actual destruction of tendon fibers. In several instances this resulted in an attenuated and elongated tendon by virtue of pseudotendon proliferation; in one instance actual tendon rupture was noted. Free floating rice bodies were noted in five of the fourteen operations. In one case of bilateral involvement rice bodies were present on one side but not on the other.

Where the tendons were involved to the extent of functional loss, repair was done at the time of operation. This consisted of tendon shortening or substitution transfers. Tendon grafts were not used. If a bone was involved, the involved portion of bone was removed if feasible. No effort was made to reconstruct the tendon sheath after the sheath was excised.

In each instance all the removed material was sent for pathologic examination, and in four cases the material was sent for bacteriologic study and guinea pig inoculation. In each instance the cultures were sterile for ordinary pathogens, and the tubercle bacilli were not isolated by smear, by culture or by guinea pig inoculation.

### PATHOLOGIC STUDY

The reports on pathologic examination of the excised material show that no fewer than seven pathologists made the diagnosis on one or more cases independent of each other. The variation in the descriptive diagnostic terms included the following: Tenosynovitis, chronic, fibrinoid; synovitis, subacute, non-specific; tenosynovitis, villous, proliferative; tenosynovitis, chronic, proliferative; tenosynovitis, chronic, rheumatoid nodule. In no case was there microscopic evidence of tuberculosis or tumor.

The general histologic descriptions were very similar to each other and included some or all of the following characteristics (Fig. 4): The tendon sheath lining was thickened; the surface was thrown into papillary or polypoid folds and was covered with a prominent layer of mesothelial cells; the stroma showed edema and vascularization with moderate infiltration of lymphocytes and plasma cells. An occasional phagocytic cell was seen, and not infrequently eosinophils were identified. In some areas fibrin with immeshed leukocytes were seen attached to the surface. The deeper layer

of the sheath was fibrous but showed edema in some cases. In one specimen (Fig. 5) a dense fibrous nodule, 3 mm. in diameter, was seen. This nodule consisted of a central zone of amorphous material bordered by a cellular layer of elongated cells in radial arrangement. This is the characteristic appearance of a rheumatoid nodule. The histologic section of a tendon shows diminution of fibrocollagenous fibers. Histologic section of a piece of muscle shows some atrophy of muscle fibers with focal increase in sarcolemma nuclei. Histologic section of involved bone was described as characteristic of chronic osteomyelitis.

### COMPOUND F IN TREATMENT

Two patients, both with bilateral involvement, after operative treatment of one side received hydrocortisone (compound F) as an injection into the involved tendon sheaths on the other side. One of the patients had flexor tendon involvement in the distal forearm and palm; the other had communis extensor tendon involvement at the wrist level. In both instances the swelling and symptoms were abolished within twenty-four to forty-eight hours. Recurrence followed in each instance, however, and the patient with flexor tendon involvement was operated upon shortly thereafter. The patient with involvement of the extensor tendon obtained relief after each injection for periods varying from two to four weeks. Injections were repeated as necessary and the condition was kept under control for eight months before surgical intervention.

Compound F was put into the surgical wound immediately after operation in three cases, and postoperative reaction and pain were appreciably reduced.

### RESULTS

Excluding one very recent case, the average time of follow-up was thirteen months. In one of the remaining ten cases there was suggestion of recurrence at the operative site five months following operation, but at the time of report recurrence was not certain. In the other nine cases there was no recurrence at the time of their last observation. Functional recovery following complete extirpation of the tendon sheath was complete, or very nearly so, in cases in which the involvement was in the distal forearm or palm or on the extensor surface at wrist level, provided there was no actual

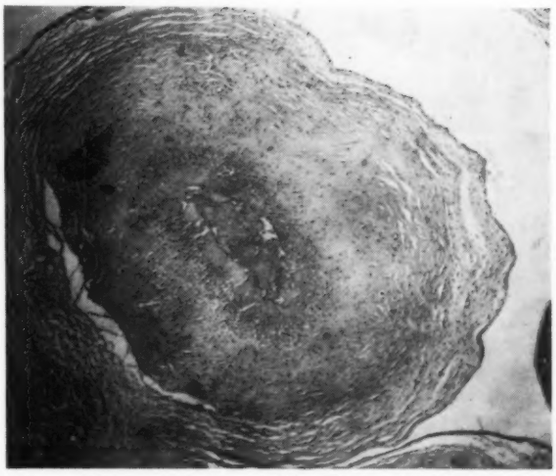


FIG. 5. Low power magnification of a rheumatoid nodule seen during microscopic study of excised tendon sheath in a case of rheumatic tenosynovitis.

tendon involvement requiring reconstructive procedures. In cases of digital flexor sheath involvement, approximately one-half of the motion was recovered—enough for most practical purposes.

### SUMMARY

Rheumatic tenosynovitis can be controlled satisfactorily by operation. The method is to remove the sheath but preserve the tendon. After such a procedure full motion often does not result but there is usually enough motion to be useful. In severe cases the tendon itself may be partially destroyed and may even rupture. In such cases it is necessary to reconstruct the tendon at the time the sheath is removed. Instilling hydrocortisone in the wound at the time of operation reduces pain considerably.

Tuberculous tenosynovitis is relatively rare; tenosynovitis should not be considered tuberculous unless there is irrefutable pathologic or bacteriologic evidence to support that diagnosis.

*Acknowledgment:* Acknowledgment is hereby made for the contribution of both material and assistance to Drs. Sterling Bunnell, Donald Pratt and William Fielder, San Francisco, Calif.

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# Embolic Grafts in the Lungs of Dogs

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THE surgeon has always been intrigued by the possibility of grafting various tissues of the body in the same or different locations in the same animal (isografts) or from an animal of the same species (homografts). In man, skin, bone, cartilage, artery and vein have successfully been used both as iso- and homografts. However, it is believed that most homografts serve only as a scaffold for the growth of the host tissue and are eventually absorbed.

Halsted postulated many years ago that the successful take of a grafted gland is to a great degree dependent upon a deficiency in the host of the secretion of that particular gland.[1] The described experiments were carried out with this in mind. A deficiency was created by the removal of thyroid, parathyroid, ovary, testicle or adrenal. A few small sections of the removed gland were marked with silver clips and introduced into the internal jugular vein creating pulmonary emboli. The site in the lung where they lodged was determined by postoperative x-ray films of the chest.

The animals were sacrificed at varying periods of time up to nine months, several earlier than was desired, as they developed distemper and it was feared pneumonitis might ensue. Before the heart and lungs were removed the bronchial circulation of six dogs was injected with a suspension of 20 per cent bismuth oxychloride in an 11 per cent solution of gum acacia. Following the removal of the heart and lungs the pulmonary circulation was injected with the same solution in nine dogs.[4] If the dogs survived over a month, no blockage of the pulmonary circulation was found. The branches of the bronchial arteries leading to the site of the grafts showed a marked dilatation. Holman and Mathes[2] demonstrated this dilatation to be present in the branches of the bronchial arteries leading to the site of an embolus.

Six dogs were embolized with thyroid. A total thyroparathyroidectomy was performed, the parathyroids being placed as free grafts in the muscles of the neck. Dog J1 was sacrificed after four days because of severe distemper and dog J4 died after forty-eight hours in convulsions probably due to parathyroid deficiency. Dogs J2, 3, 5 and 6 were sacrificed at nine months, eight weeks, six weeks and fifteen weeks, respectively. Convulsions were controlled by administering calcium chloride by vein or stomach tube. J2 required no calcium while it was necessary to administer calcium to J6 for thirty-three days. In all of the last four dogs, J2, 3, 5 and 6, functioning acini were found. (Figs. 1 to 3.)

Bilateral oophorectomy was performed in two animals. Dog J7 was sacrificed in six weeks at which time viable ovarian tissue was found. (Fig. 4.) Dog J17 was sacrificed in five months but no ovarian tissue was found.

Bilateral orchiectomy was performed on two animals. Dog J8, sacrificed in six and one-half months, showed living testicular tissue. (Fig. 5.) In dog J18, sacrificed in four and one-half months, no living tissue was found. However, there was an interesting finding in connection with this dog. Most of the grafts were marked with a fine silver clip so that the location of the grafts could be seen in the x-ray films. This chanced to be one of the dogs subjected to bronchial artery injection which had constantly revealed dilatation of the branches leading to the site of the graft. In this single instance the bronchial arterial branches leading to a different site in the lobe than where the clip was lodged were dilated. It is possible that the clip became separated from the graft and that there was a living graft although it could not be located.

Two animals, J11 and J14, were subjected to bilateral adrenalectomy. J11 was done in one stage and lived only an hour. J14 was done in three stages over a period of twenty days but lived only one day postoperatively. These were done in the pre-cortisone days.

One animal, J10, was embolized with parathyroid. Convulsions were controlled for one month by oral calcium after which it was dis-

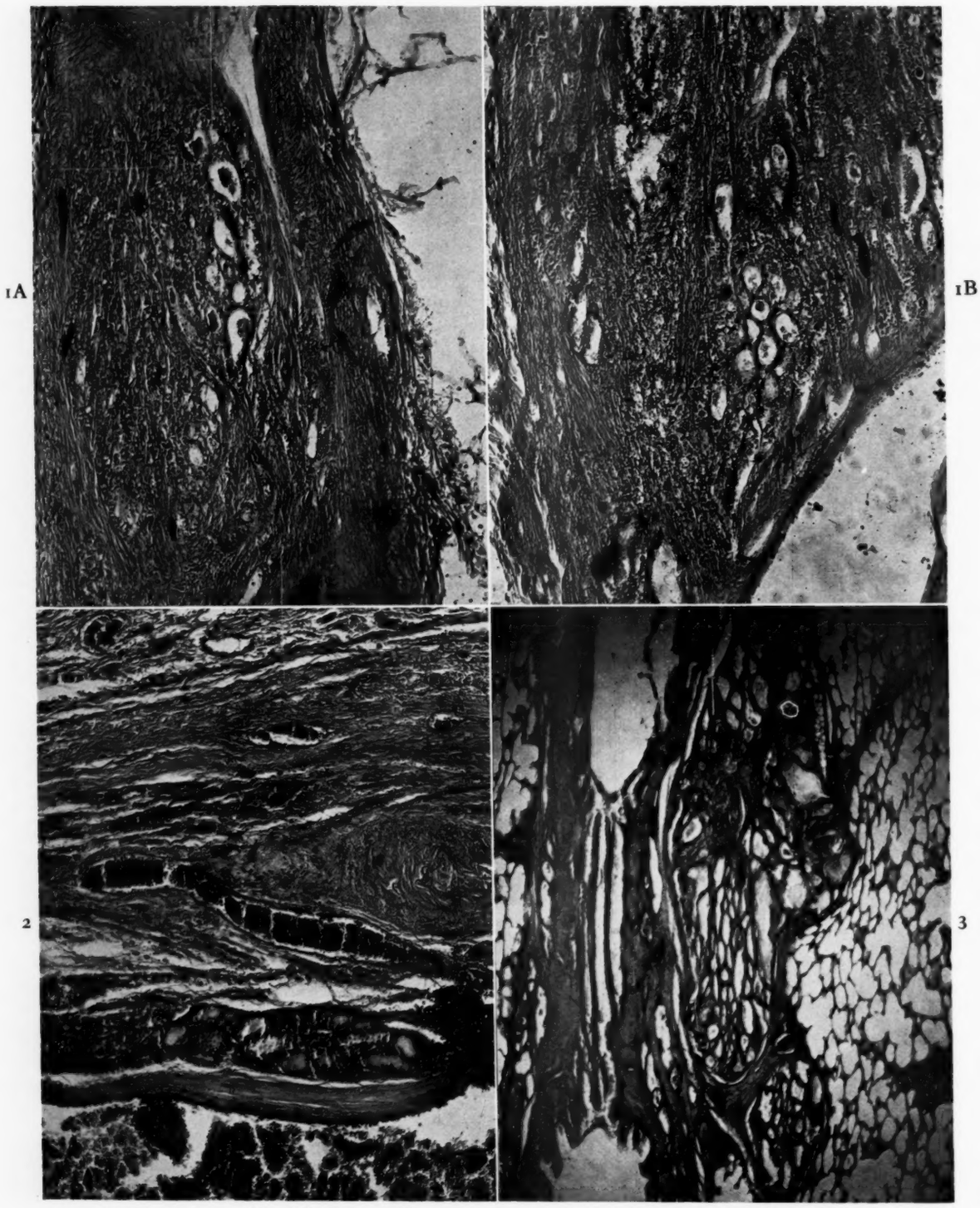
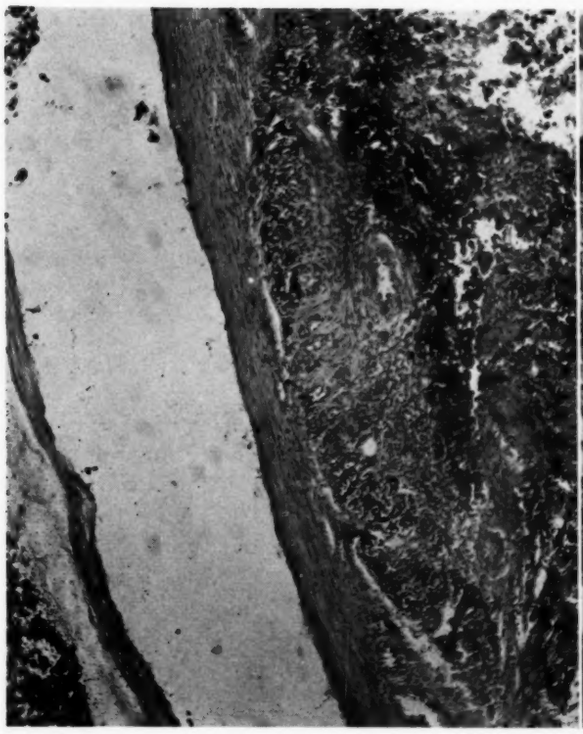



FIG. 1. A, dog J2, lung (thyroid). Lumen of pulmonary artery is occluded by thyroid glandular tissue which is viable. Although a number of acini are collapsed, others contain colloid and their lining, cuboidal, epithelial cells, show good nuclear staining. Irregular masses of black material in the section are representative of bismuth oxychloride emulsion injected at the time of autopsy following sacrifice of animal. B, higher magnification.

FIG. 2. Dog J3, lung (thyroid). In the adventitia of medium-sized pulmonary artery there is a linear zone of viable thyroid glandular tissue, many of whose acini are well laden with colloid; nuclear staining is good.

FIG. 3. Dog J5, lung (thyroid). Situated between the adventitia of a small pulmonary artery and contiguous branch of small bronchiole is an island of thyroid glandular tissue bounded partially by pulmonary alveolar parenchyma. Acini for the most part are well filled with colloid and lined by epithelial cells showing good nuclear staining.



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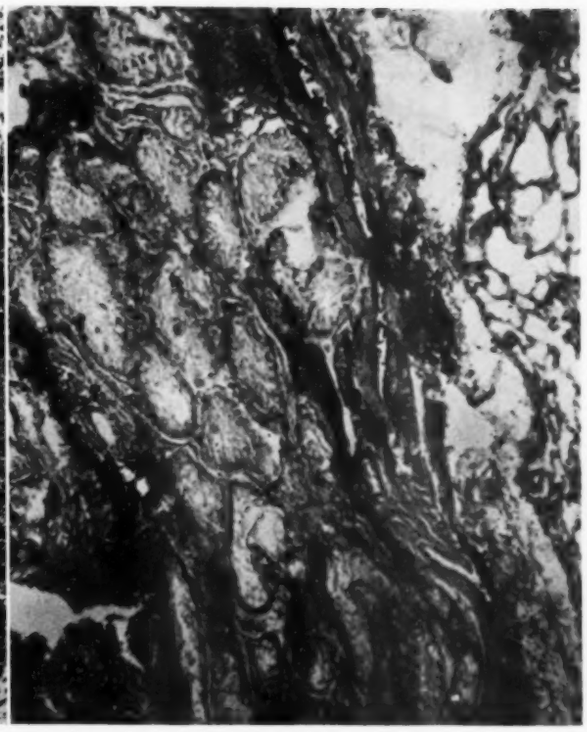

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FIG. 4. Dog J7, lung (ovary). In the adventitia of a medium-sized pulmonary artery is an island of viable tissue which has shown differentiation toward formation of tubules. Nuclear staining is good.

FIG. 5. Dog J8, lung (testicle). Filling the lumen of a medium-sized pulmonary artery is an embolus consisting of testicular tissue. The outline of spermatogenic tubules is distinct. The only remaining viable cells are those of Sertoli. Spermatogonia, spermatocytes and spermatids are not apparent. Interstitial cells of Leydig are not identified.

continued. The dog died at the end of five months in a seizure of convulsions. No living graft could be found.

Four animals were subjected to testicular homografts. Dogs J12 and 13 died in six and eight days, respectively, of what was interpreted as anaphylactic shock. Dogs J15 and 16 were found to have compatible blood before a similar procedure. J15 escaped from the kennels after twenty-four days and J16 was sacrificed at the end of five months. No viable graft was found.

## CONCLUSIONS

1. Emboli of thyroid, ovary and testicle have been shown to grow as isografts in the lung.
2. There is dilatation of the branches of the bronchial artery to the site of the grafts.
3. Homografts were unsuccessful.

*Acknowledgment:* I am indebted to Dr. David A. Wood for selecting and captioning the slides for photomicrographing.

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# Iliac Thrombophlebitis—Visualization Prior to Ligation

CASE REPORT

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ALTHOUGH a vast amount of literature has accumulated on the treatment of venous thrombosis in the extremities associated with pulmonary emboli, much difference of opinion still remains regarding the specific treatment for any given case.

Anticoagulant therapy with heparin and dicumarol has many advocates and is used extensively in this condition, but surgical vein interruption has become a practical mode of management in certain instances. The extent to which surgery is utilized depends in part on the enthusiasm of the operators.

The types of operative procedures for the treatment of iliac and vena caval obstruction have been carefully reviewed by several authors during the last decade. In 1943, Shackelford reported a good result in a case similar to the one presented here. Homans discussed the subject completely and reported fourteen cases of iliac vein exploration and ligation, the right iliac on six occasions and the left iliac on eight. He prefers the extraperitoneal approach because of the ease of operation and diminished postoperative complications. Moses reported twenty-one cases of iliac ligation along with fifteen cases of inferior vena caval ligation, with a mortality of 37 per cent. Many of his patients, however, were moribund at the time of operation. All authors note the relative inaccessibility of the left common iliac vein because of its anatomic position behind the artery, making mobilization difficult and sometimes hazardous.

More recently, interest has turned to ligation of the inferior vena cava in preference to ligation of the iliac veins. This is due in part to failures following a unilateral ligation, with subsequent emboli, plus the observations of Ray and Burch, Rentz, Veal, and others that caval ligation below the renal veins leaves few, if any, sequelae and is quite compatible with life. The technical procedure again employs a right-sided extraperitoneal approach, which affords visibility of the inferior vena cava sufficient for ligation. Sympathectomy can be combined easily with ligation since the lumbar chain is quite accessible through either the intraperitoneal or extraperitoneal approach.

Visualization of the inferior vena cava by x-ray was reported in 1947, by O'Loughlin. In fifty patients, "cavograms" were obtained by the injection of 20 cc. of 35 per cent diodrast into the femoral vein. No sequelae were noted, although in one patient the diodrast escaped into the surrounding tissues.

In the case report to follow, it was believed that the patient would be unsatisfactory for anticoagulants because of the bleeding tendency associated with ulcerative colitis.

### CASE REPORT

A thirty-seven year old white farmer entered the hospital on June 4, 1949, because of recurrent symptoms of idiopathic ulcerative colitis. He had first been observed and treated for this disease in 1943, while on active duty in New Zealand. The condition improved after one month and he had no serious disability until 1945 when he again had an exacerbation lasting five months. The current episode began one month prior to entry, when he began having six bowel movements daily, which had increased to ten to twelve at the time of entry, accompanied by a weight loss of 15 pounds. Past history and family history were non-contributory.

Physical examination showed a well developed, undernourished male who appeared older than his stated age. The physical examination was otherwise essentially normal, except for a well healed McBurney scar.

Laboratory studies revealed the following: red blood cells, 4,350,000; hemoglobin, 13.5 gm. per cent; white blood cells, 20,500; poly-

morphonuclears 74, lymphocytes 23, eosinophils 2, monocytes 1; erythrocyte sedimentation rate 14; urine essentially negative. Stool examination showed no ova or parasites and ++ occult blood. Liver function tests revealed thymol turbidity of 5.5, alkaline phosphatase 22.5 King-Armstrong units, zinc turbidity 14.6 units. Proctoscopy to 22 cm. demonstrated pale mucosa which bled easily. No ulcerations were seen.

X-ray studies showed evidence of ulcerative colitis involving the splenic flexure and descending colon.

The patient was placed on a conservative regimen to control the diarrhea, and other symptomatic treatment was instituted. On June 8th, a sudden episode of severe right pleural pain occurred accompanied by a small amount of blood-tinged sputum. Physical signs showed evidence of probable pulmonary infarct, which was confirmed by x-ray. An intensive examination of the extremities was made, but no evidence of venous thrombosis could be detected.

During the ensuing week the pleural pain completely disappeared and the patient was improving satisfactorily until July 1st when he again had a similar attack of left-sided pleuritic pain associated with increased respiratory rate and hemoptysis due to an infarct in the left lower lobe. Again, an intensive search for possible sources of the infarct failed to show a definite site.

On July 6th a rather sudden aching pain developed in the patient's left groin and leg, which became quite severe during the ensuing three hours. The leg, which had been previously normal in size and appearance, became swollen and tender, and there was marked distention of the veins of the thigh, including the saphenous. The tenderness and cyanosis of the left leg extended above the groin, and tenderness could be elicited in the left lower quadrant. A diagnosis of iliac thrombophlebitis was made. Prothrombin time was reported as 80 per cent of normal. There was no evidence of any involvement of the right leg. Because of the presence of active ulcerative colitis, it was believed that anticoagulants were contraindicated, and venous interruption was recommended.

Accordingly, that afternoon, a midline incision was made above and below the umbilicus and transperitoneal exploration of the left common iliac vein was done. The proximal portion of the left common iliac was soft and showed no evidence of inflammation, but a clot was palpable in the vein at its bifurcation. Inflammation and edema of the distal end of the left common iliac vein and the proximal portions of its two main branches were noted. The right iliac was essentially normal. In an attempt to visualize the site of venous obstruction, 20 cc. of 35 per cent diodrast were injected into the left common iliac after temporary proximal occlusion of the vein, and x-rays were taken which showed a block at the bifurcation of the common iliac. The left common iliac was mobilized, divided at its junction with the inferior vena cava, and the ends ligated and transfixed. The sympathetic ganglia of L-2 and 3 were removed on the left side through this approach. The posterior peritoneum was closed and the abdomen was closed in layers.

FIG. 1. Infra-red photograph showing collateral circulation around the thigh and the superficial abdominal vessels, after ligation of the left common iliac.

Postoperatively, the patient was confined to bed in the horizontal position with both legs wrapped in Ace bandages to the groin. On the second postoperative day the patient was allowed out of bed. By the third day, the left leg was still swollen with residual tenderness

FIG. 2. Phlebograms of left saphenous vein with no filling of the iliac veins.

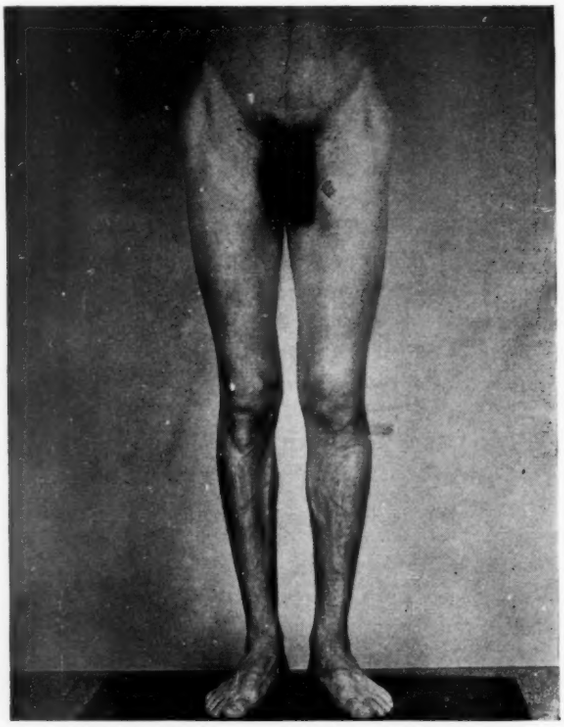

FIG. 3. Minimal edema six weeks postoperatively.

over the superficial veins, but the edema had increased. Measurements of the leg at that time showed an increase in size of about 1 inch on the involved side. Two weeks postoperatively, the left leg had returned essentially to normal size and there was obvious increase in the collateral circulation over the upper thigh and groin as well as through the superficial abdominal vessels. These are clearly visualized by the infra-red photograph. (Fig. 1.) One month postoperatively comparative measurements showed only ½ inch increase in circumference on the left side. Phlebograms taken on August 30th, six weeks postoperatively, showed the saphenous vein well with no visualization of the deep system. (Fig. 2.)

The patient's hospitalization was continued until September 2nd, for treatment of the ulcerative colitis, which consistently improved under medical management. He is now completely ambulatory, with minimal edema and moderate fatigue of the leg after exercise. (Fig. 3.) There have been no further pulmonary infarcts.

## COMMENTS

The late disability resulting from ligation of either the common iliac or the inferior vena cava is vastly different from that following ligation of the common femoral. With the latter, chronic edema, trophic skin changes and ulceration are noted, leading to significant functional impairment and disability. With higher ligations, however, the incidence of crippling sequelae is minimal, and in a high percentage of cases there is only slight residual swelling and no subjective complaint.

Ordinarily, the extraperitoneal approach is considered preferable for iliac and inferior vena caval interruptions. By this technic the right common iliac and inferior vena cava are approached from the right side and the left common iliac from the left side. In this case, however, the transperitoneal exploration was selected in order to visualize adequately both the inferior vena cava and the left common iliac and to permit the appropriate ligation.

The selection of the site for ligation depends logically upon the extent of the thrombotic process, which may be difficult to ascertain in certain circumstances.

Palpation of the vein is helpful in determining the level at which ligation is preferable, but this method is subject to some degree of unreliability because of difficulty in feeling soft clots within the vein.

It occurred to us that the use of retrograde visualization of the venous tree might be of some value in determining the extent of the thrombosis. Twenty cc. of 35 per cent diodrast were injected into the common iliac vein after temporary proximal occlusion of the vein, and

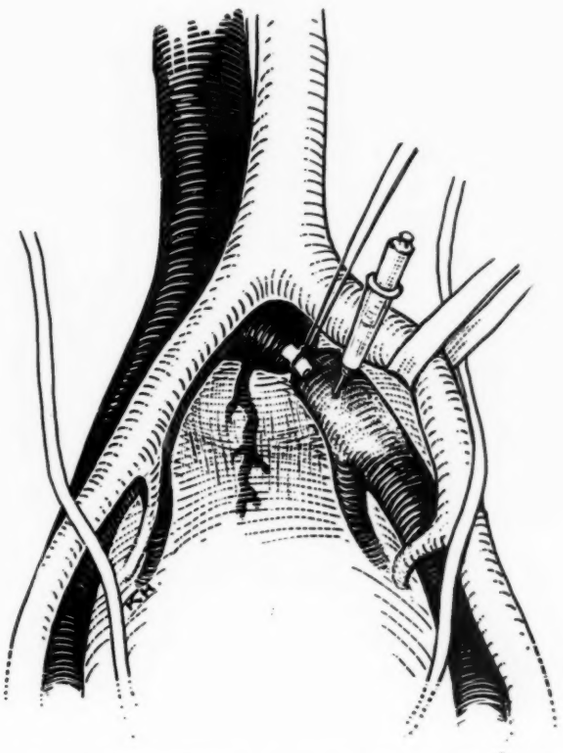

FIG. 4. Shows drawing of temporarily occluded left common iliac vein and syringe for injection of diodrast. Light area indicates dye in the vein conforming to the x-ray seen in Figure 5.

an x-ray taken at that time showed the site of obstruction to be at the junction of the internal and external iliac veins. (Figs. 4 and 5.) This procedure does assure one that the clot has not progressed beyond the proposed site of interruption, and in this case led to ligation and division of the common iliac in preference to the vena cava.

The ipsilateral sympathetic chain is easily accessible by extending the incision in the posterior parietal peritoneum upward along the great vessels. The value of this additional maneuver is obviously difficult to assess with one report. However, it may contribute to a more prompt return to normal of the vascular tree after venous interruption.

FIG. 5. X-ray taken during operation showing diodrast in common iliac vein, and obstruction of internal and external iliac veins.

## CONCLUSION

1. A case report of iliac thrombophlebitis with embolism is presented, with treatment by ligation and division of the left common iliac.
2. The site of venous obstruction was visualized by x-ray at the time of operation.
3. Sympathectomy can be combined with the procedure of venous interruption and may be an adjunct to return of the extremity to normal.

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# Surgical Significance of Gastrointestinal Bleeding

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GROSS bleeding from the gastrointestinal tract still proposes a difficult diagnostic and therapeutic problem. Despite the tremendous literature that has accumulated through the years on this perplexing problem, opinion as regards management continues to be divided, even when the source of bleeding has been demonstrated.

Whereas alarming hemorrhage from the gastrointestinal tract is occasionally encountered as the result of lesions of the small bowel below the ligament of Treitz and also at times from lesions of the large bowel, these are relatively infrequent and, in our experience, seldom end fatally. On the other hand, bleeding peptic ulcer and esophageal varices are a common cause of exsanguination and frequently cause death. Our major problem, therefore, both as regards diagnosis and therapy, involves mainly the esophagus, stomach and duodenum. There are three main reasons for the confusion that still exists concerning both diagnosis and therapy: (1) lack of experience on the part of most physicians in the management of this condition; (2) the wide divergencies of mortality statistics which appear in connection with the various forms of therapy recommended in the literature; and (3) the difficulty so frequently experienced in determining the source of bleeding. The major interest in this problem is centered in large teaching institutions, particularly in those that receive a number of emergencies because of an attached emergency ambulance service. Outside of large institutions these cases fortunately are rare enough so that few persons have a wide experience with them. It is not strange then that few private physicians see a sufficient number of acute cases of gastrointestinal bleeding to consider their management a serious problem. Most large institutions, however, are confronted constantly with the problem and report a variety of methods of management. Evaluation of these methods as presented in the literature is hampered because of the variable criteria which have been utilized for the inclusion or exclusion of certain cases. The reported mortality figures for hemorrhage vary from 1 to 40 per cent. It is obvious that this great discrepancy must indicate that the various authors are not reporting a comparable series of cases. Also, a good many patients die from gastrointestinal hemorrhage, the source of which is never determined.

Little unanimity of opinion exists as to what constitutes massive hemorrhage. Gross hemorrhage of mild degree often has been placed in the same category with massive hemorrhage resulting in exsanguination, shock and death. All ulcerating lesions of the mucous membrane of the gastrointestinal tract bleed to a lesser or greater degree; some so minutely that the effects are difficult to detect and some so acutely and grossly that they cause almost immediate exsanguination and death. Until some standard has been devised to determine accurately the relationship between the degree of hemorrhage and mortality, both as regards the amount and the duration, confusion will continue to exist in the evaluation of various forms of therapy. Meulengracht,[1] for example, in a discussion of bleeding peptic ulcer, included in his series all patients who had any evidence of gross bleeding (visible melena or blood in the vomitus). He reports a mortality of 2.5 per cent, whereas Stewart and co-workers,[2] considering only massive hemorrhage sufficient to produce shock, note a 29 per cent mortality. Chiesman[3] finds the mortality of all patients who entered with massive hemorrhage of over forty-eight hours' duration to be 74 per cent.

These grossly conflicting figures serve only to emphasize the importance of a definition of massive hemorrhage before the effectiveness of various types of therapy can be evaluated.

We consider massive gastrointestinal hemorrhage that amount of bleeding sufficient to

cause sudden weakness, dizziness or syncope, often almost immediately followed by vomiting of a large amount of blood, or by the passage of a large tarry stool, and often by both. The victim is pale, cold and sweating, slightly cyanotic, restless and thirsty. The pulse is small and rapid, usually over 120 per minute; the systolic pressure is usually below 90. Blood counts and hemoglobin determinations are low, but are not necessarily an index of the blood loss at this stage. A low hemoglobin and low erythrocyte count certainly mean bleeding of significant proportions, but they are not necessarily indicative of the acute profuse type which the term massive implies and in which there is an immediate threat to life.

Hematemesis is a frequent but not constant finding in acute exsanguinating hemorrhage from the upper gastrointestinal tract. In our experience, the vomiting of blood most certainly means bleeding from a point above the ligament of Treitz; however, the absence of hematemesis does not rule this out. Massive bleeding into the stomach or duodenum may cause violent peristalsis with the rapid passage of almost unchanged blood into the stool. Bright red blood passed by rectum, therefore, does not have its origin in the lower gastrointestinal tract necessarily, but actually may be indicative of upper gastrointestinal bleeding.

The cause of gastrointestinal bleeding often proposes a most difficult diagnostic problem which occasionally cannot be determined accurately. Patients present themselves to the physician in all stages of reaction to hemorrhage. Frequently those in the greatest need of an accurate diagnosis and early treatment are the least able to give an accurate history. Usually it is not difficult to distinguish between upper and lower tract bleeding whereas it is frequently impossible to be certain of the exact source in either category. If the source is not evident from the history, clinical findings and previous roentgenograms, an x-ray examination during the acute stage of bleeding may be indicated. Welch[4] of Boston believes that early roentgenologic examination by Hampton's[5] technic is advisable in all questionable cases. He reports a positive diagnosis of ulcer in 85 per cent of the cases in which it was used.

Gastric, duodenal or anastomotic ulcers in our experience are responsible for only about 50 per cent of the gross hemorrhages from the upper gastrointestinal tract. About 50 per cent come from other lesions, such as esophageal varices, gastric neoplasms, acute gastritis, benign tumors and aneurysms. Fatal hemorrhage usually originates from esophageal varices or from erosion of a large artery, usually the superior pancreaticoduodenal, the right or left gastric or their major branches. Occasionally a ruptured aneurysm may be the cause of death. The eroded stoma of a sclerotic vessel generally is found fixed in the base of an ulcer crater surrounded by dense scar tissue from which it cannot retract. Occasionally, however, ulceration may not be a prominent feature, the bleeding vessel being concealed in folds of mucous membrane.

Persistent slow bleeding usually comes from the erosion of smaller vessels in the submucosal plexus.

Unfortunately, there are no certain criteria upon which one can base a definite prognosis in any given patient. There seem to be, however, several significant observations on which there is more or less general agreement. There can be little doubt that the mortality risk of hemorrhage from ulcer increases with the age of the patient. In patients under forty-five years of age the death rate from hemorrhage is low, whereas it increases rapidly thereafter. There seems to be a definite correlation between the existence of arteriosclerosis and bleeding. Postmortem examinations in young individuals who have bled to death frequently have shown the presence of an arteriosclerotic plaque in the vessel from which exsanguination took place. This is more commonly true in the old age groups and probably is one of the main reasons why uncontrollable hemorrhage increases with advancing age.

Although it is often impossible to localize the bleeding point during the active stage of hemorrhage, it has been demonstrated that the location of an ulcer in reference to an adjacent major artery is the determining factor as regards the extent and seriousness of bleeding. The mortality from gastric hemorrhage is higher than that due to duodenal ulcer, apparently because massive hemorrhage from gastric ulcer nearly always is due to an erosion of the right or left gastric artery while bleeding from the duodenum frequently is from small submucosal vessels rather than from the gastroduodenal or pancreaticoduodenal artery.

An exact determination of the duration of bleeding also is difficult to determine but is of grave prognostic importance, as is the occurrence of persistent or repeated bleeding in the patient under observation. Patients may be unaware of bleeding of long duration which has been sufficient to cause severe secondary anemia and they report for treatment only after sudden gross hemorrhage superimposed on the profound secondary anemia has reduced the circulating blood volume to a critical level.

Massive hemorrhage brought under control by the administration of blood by transfusion in our experience is apt to recur suddenly and end fatally. Severe recurrent bleeding is most apt to occur within the first three days after the initial hemorrhage, but cannot be depended upon as a rule. Hemorrhage that continues massively and persistently after entry to the hospital is almost universally fatal unless the patient is subjected to an operation during the critical stage of bleeding.

Surgical intervention, if it is to be undertaken, should be carried out early in the episode of bleeding or its recurrence. Adequate evidence has been accumulated that delay beyond a forty-eight-hour period increases the operative mortality to a prohibitive degree.

It has been stated that the number of previous hemorrhages is important in the determination of possible exsanguination and death. When one considers the number of patients who bleed to death at home without the benefit of medical aid and those who have bled significantly and have recovered without hospital care, it becomes evident that an accurate figure concerning this factor cannot be determined and certainly is not of major importance.

Complicating diseases such as coronary thrombosis, cerebral thrombosis, tuberculosis, pneumonia and heart or kidney disease are encountered frequently and probably affect prognosis to a degree, but in the light of collected experience are not to be considered too seriously. Acute and chronic alcoholism, in our experience, affect the outcome more seriously than do the other conditions.

In view of the conflicting reports in the literature, the inherent difficulties in diagnosis and the ever present danger of exsanguination in patients over forty-five years of age, what policy of management should be adopted? There are three methods to be considered: (1) conservative medical management of all cases regardless of age, duration or amount of bleeding; (2) early operative intervention in all patients who are thought to be bleeding from a gastric or duodenal ulcer or neoplasm; and (3) careful selection of patients for each of these methods of treatment. It has been our belief for some time that each physician and each institution should adopt a policy of treatment commensurate with the facilities and personnel available to them and that the internist and surgeon should work together and not at cross purposes, which can lead only to disaster for the patient. It is clear that the methods of management must vary and that those applicable in one institution cannot always be applied in another. The introduction of surgery as a means of treatment presupposes a team skilled in diagnosis, resuscitation, anesthesia and surgical technic, while the conservative medical management of all bleeders, to be reasonably successful, requires proper laboratory facilities and the availability of sufficient quantities of whole blood.

The method that we have adopted may be described briefly as follows: On admission, a suspected case of acute gastrointestinal bleeding is seen jointly by a competent internist and the resident surgeon, who is capable of carrying out emergency radical surgery if deemed advisable. Blood studies are made at once, including determinations to rule out hemorrhagic diathesis and primary blood diseases. A slow drip blood transfusion is started in one or more veins and the rate of flow regulated according to the clinical estimate of the rate of blood loss. A chart is started at once recording pulse rate, blood pressure, hemoglobin and hematocrit determinations. The pulse and blood pressure are recorded every fifteen minutes. An attempt is made to record a careful and accurate history concerning previous health, digestive disturbances, source of hemorrhage, amount of blood lost, time of bleeding and interval before admission. On examination, pallor, restlessness, sweating, disorientation and dehydration are looked for. Unnecessary movement of the patient is avoided and abdominal palpation is undertaken with a great deal of care.

In making the first assessment of the patient on admission, evidence of severe or continuing blood loss is obtained best by noting the clinical signs of pallor, restlessness and sweating. After

a baseline has been established, changes in pulse rate and blood pressure seem to us to be the most accurate guide to the patient's condition.

After admission the patient must be watched without interruption. We have used morphine in small amounts to control restlessness and apprehension. An inlying Levine tube may be helpful as a means of removing blood clot and hydrochloric acid from the stomach, but is not particularly valuable in determining the state of bleeding. We object to feeding mainly because of the danger of aspiration if surgery is undertaken early.

Careful and constant observation are necessary so that continued or recurrent hemorrhage may be recognized promptly. We have found the pulse and blood pressure chart the most helpful routine observation for this purpose. The hematocrit and hemoglobin determination are useful adjuncts. Not only should the pulse rate remain steady, but it also should come down gradually to less than 90 per minute if the progress is to be accepted as adequate. As the pulse diminishes the blood pressure should rise to a level of at least 100 systolic and then maintain itself.

Stabilization will nearly always occur with two or three 500 cc. transfusions of whole blood.

A tendency to sweat about the head often is an early sign of renewed bleeding and may be observed before signs of restlessness and dehydration are evident. Pallor may or may not be obvious.

If bleeding is slight, but persistent, there may be no other evidence than a fall in the hemoglobin level or failure of the level to rise despite the giving of blood.

Failure to respond to whole blood transfusions, in our minds, is the major indication for early surgical intervention. If after three consecutive transfusions the patient does not stabilize, surgery is advised and is to be undertaken immediately.

If stabilization occurs and sudden bleeding recurs, blood replacement is carried on very rapidly and surgery advised.

When stabilization occurs and can be maintained by intermittent blood transfusions, conservative medical management is continued. These patients can be built up rapidly and then considered for interval resection.

Although we do not advocate the surgical management of all peptic ulcers, we do believe that massive gastrointestinal hemorrhage in patients over forty-five years of age is a definite indication for gastric resection.

When the decision to operate is made in an acute case of bleeding, the rate of blood inflow is increased and blood is given continuously. An attempt is made to evacuate the stomach by suction on the nasogastric tube.

Intratracheal anesthesia is preferred mainly to prevent aspiration of blood into the trachea. Because of this danger, constant suction is maintained on the gastric tube during and immediately after induction. Occasionally we have found it difficult to persuade the anesthesiologist to proceed with anesthesia because of the patient's condition resulting from severe blood loss. However, on more than one occasion we have been able to revive a more or less moribund patient by the rapid administration of blood after bleeding has been controlled by local pressure on the exposed bleeding point.

The surgical problem is to stop bleeding. It is necessary, therefore, to work quickly but gently until the bleeding vessel has been secured. If the source of bleeding is not obvious from rapid inspection after the abdomen has been opened, time should not be wasted by prolonged exploration outside the gastrointestinal tract. The great majority of severe hemorrhages occur from erosions on the posterior wall of the duodenum or on the lesser curvature of the stomach. We prefer to open the antral portion of the anterior wall of the stomach rather widely so that blood can be removed from these areas thoroughly and quickly, and a direct inspection carried out. When a bleeding point is encountered, it should be stopped immediately by pressure and nothing more undertaken until a sufficient amount of blood has been given under pressure to restore the blood pressure to a point above shock level. The open inspection of the stomach and duodenum, the control of hemorrhage by pressure and the restoration of blood pressure by rapid transfusion before further manipulation within the abdomen takes place are the three most important maneuvers at the time of surgery.

After restoration of the blood pressure one may proceed with an elective procedure. In the presence of chronic peptic ulcer, partial gastrectomy is the operation of choice. It not only solves the immediate problem of bleeding, but also leaves the patient in a satisfactory

position for future life. Partial gastrectomy in the presence of gastric ulcer is almost always feasible. In chronic duodenal ulcer the problem may be technically difficult, particularly when the ulcer is too far removed from the pylorus to warrant safe removal. We have not hesitated under these conditions to leave the ulcer *in situ*. Only when the bleeding was obviously from an erosion of the gastroduodenal artery have we ligated this vessel outside the ulcer bed and then only when the ulcer was not resected.

Bleeding under other circumstances is controlled by resection of the ulcer. Occasionally we have found it advisable to leave a penetrating ulcer of the pancreas in place after dissecting the walls of the stomach or duodenum away from it. A suture in the base of the ulcer under these circumstances may be necessary to control bleeding. Ordinarily we prefer not to ligate vessels in the base of the ulcer, particularly if the ulcer remains within the lumen of the gastrointestinal tract, because of the danger of digestion and secondary hemorrhage. Ligation of the vessel in the ulcer bed and gastroenterostomy as the method of treatment to save time is to be condemned, in our opinion, because of this danger.

On occasion careful inspection of the stomach and duodenum does not reveal the source of bleeding. Opinions as to how to proceed under these circumstances differ greatly. We have at times elected to carry out a resection under these circumstances, but more often than not have experienced recurrence of the bleeding. On two occasions in our early experience patients treated by resection without evident cause died as the result of subsequent massive hemorrhage from ulcers discovered at autopsy to be remaining in the proximal gastric stump. More recently one patient proved subsequently to be bleeding from an aneurysm of the hepatic artery, another from an aneurysm of the splenic artery, and a third from a carcinoma of the tail of the pancreas.

On The Stanford University Surgical Service at the San Francisco Hospital during the five-year period from 1947 through 1952, 215 patients were admitted because of massive gastrointestinal hemorrhage. Of these, seventy-one died, an over-all mortality of 33 per cent. Ninety-seven, or 45 per cent, of the total proved to have peptic ulcers; sixty-four duodenal, twenty-seven gastric and six marginal. A total of twelve patients with proven ulcers died (six duodenal and six gastric), a mortality of 12.3 per cent.

Sixty-seven of the 215 bleeders proved to have esophageal varices and of these, forty-seven died (mortality of 66.3 per cent). The source of bleeding was not determined in forty-seven patients and of these, thirteen died (mortality of 27.7 per cent). One death resulted from gastric carcinoma and one from esophageal ulcer.

Twenty-one patients were operated upon during the acute stage of bleeding, with one death resulting on the third postoperative day due to myocardial infarction; the operative mortality was 4.8 per cent. We believe that had these patients not been operated upon during the acute stage of bleeding, they most probably would have bled to death. This assumption being true, there would have been thirty-three instead of twelve deaths in the ulcer group, which would have raised the mortality to a figure approximating that of the over-all mortality of 33 per cent.

## SUMMARY AND CONCLUSIONS

The mortality from massive gastrointestinal hemorrhage is still alarmingly high. In 215 cases studied at the San Francisco Hospital during the years 1947–1952, the over-all mortality was 33 per cent. The mortality from proven gastric or duodenal ulcer was 12.3 per cent.

Fatal gastrointestinal bleeding almost invariably has its source above the ligament of Treitz and can be controlled adequately in carefully selected cases by emergency surgery during the acute stage of bleeding. Emergency surgery is indicated in a selected group of patients who do not respond to conservative measures and in those who have recurrent bleeding while under observation.

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# Subtotal Gastric Resection for Peptic Ulcer

## HISTORICAL REVIEW WITH THE DESCRIPTION OF A VARIATION IN TECHNIC

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IN the past seventy-odd years subtotal gastric resection has retained a favored position in the surgical treatment of peptic ulcer. True, it has had its ups and downs as concepts of the nature of the disease have changed and as various technical procedures have been introduced and tested by those strict but impartial judges, experience and time. The purpose of this paper is to tell the story of the development of subtotal gastric resection as it relates to the treatment of peptic ulcer and to describe an operation which applies the lessons learned. It is well to review the experience of the past for it has brought us to the present and is our best guide into the future.

Billroth[1] performed the first successful subtotal gastrectomy for carcinoma of the pylorus in 1881. In 1885 von Hacker[24] reviewed the resections performed at Billroth's clinic and found several specimens to be benign strictures. Thus the first resections for ulcer were done according to the Billroth I method, a method which is receiving new popularity today. The Billroth II operation was also applied to the treatment of benign ulceration with stricture. The two basic principles of subtotal gastric resection were used from the very beginning in the surgical treatment of peptic ulcer. These early operations were performed to remove the obstructing lesion and to restore the continuity of the gastrointestinal tract. The underlying causes of the disease were not well understood; hence no conscious effort was made to correct them surgically.

In 1881 Billroth's assistant, Woffler,[26] performed the first short circuiting operation of gastroenterostomy. In 1886 Heineke and Mikulicz devised a method of local excision and enlargement of the stenosed lumen of the pylorus. At that time these operations were so much simpler and were attended with so much less risk to the patient that they quickly replaced the more formidable operation of resection for benign ulcers and strictures.

Gastroenterostomy gave good results initially in benign strictures of the duodenal cap and pylorus and was relatively easy to perform, so that its popularity rose rapidly. Plastic procedures had a temporary vogue but were never widely accepted. Under the stimulus of Moynihan's endorsement in England and the Mayos and other surgeons in America a tremendous number of gastroenterostomies were performed for peptic ulcer during the first quarter of this century. In the hands of conscientious, conservative surgeons the inherent faults in the method were slow to appear. More enthusiastic and less careful operators widened the indications for gastroenterostomy and then its faults became apparent. Chief among these was the occurrence of secondary jejunal ulceration, often with bleeding or perforation into the colon or into the peritoneal cavity. Frequently the patient was much worse off than he had been with his relatively mild original disease.

The poor results of gastroenterostomy led to the reintroduction of subtotal gastric resection as a method of treating patients with ulcers. During the 1920's the larger surgical clinics here and abroad were literally flooded with patients suffering from recurrent gastrojejunal ulceration. In many of these patients the only operation which could be performed was subtotal gastric resection. Meanwhile a few surgeons had continued to perform primary subtotal resections as the operation of choice for both duodenal and gastric ulcers. Notable among these were Lewisohn,[14,15] Finsterer[12,13] and von Haberer.[21–23] The type of operation then being performed was limited to antral resection; however, it was soon found that some of these patients also returned with secondary jejunal ulcers. In these patients, the bridges for less radical methods having been demolished, nothing remained but to perform a still higher resection. As more and more

stomach was removed, it finally became evident that at a certain point secondary ulceration no longer occurred. During this period one less radical method was tried and found wanting. This was the exclusion operation of von Eiselsberg[20] and of Devine.[8] In this operation the distal portion of the stomach was cut across and closed but not removed. The proximal portion of the stomach was then anastomosed to the jejunum. Patients so treated almost immediately developed severe secondary ulcers so that fortunately the method was short-lived. As a result of all this clinical experience it became evident that both the antrum and a large part of the body of the stomach had to be removed in order to prevent recurrent ulceration.

At this point something should be said as to how concepts of the nature of the disease and its causes were developing. It appeared obvious from the beginning that the acid-pepsin digestive juices must play some part in ulcer formation. Also, it was apparent that some factor or factors must render localized areas of mucosa, normally resistant to the action of these juices, vulnerable to digestion by them. Early concepts dealt largely with these latter factors. Endarteritis, arterial spasm, trauma, infection, and neurogenic and psychic causes all had their adherents and were explored and discussed at length.

Mann and Williamson,[16] operating on dogs, demonstrated that emptying the stomach contents directly into the jejunum and short circuiting the duodenum and its normally alkaline contents invariably resulted in chronic ulceration. The ulcers so formed resembled exactly chronic duodenal ulcer in man. This was true of their gross and microscopic appearance and their tendency to bleed and perforate.

Later it was found that ulcers could be produced in many laboratory animals by causing a continuous and excessive secretion of acid-pepsin digestive juices. This was done by injection of histamine in beeswax. Countless experiments have been made and an immense literature has accumulated around these experiments. Recently Cheney[3] has demonstrated an ulcer-preventing and healing factor, vitamin U, which opens a new approach to the ulcer problem. One conclusion, not new but firmly established on the basis of clinical experience and laboratory investigation, is that excessive secretion of acid-pepsin digestive juice is an essential factor in the formation of ulcer.

It can now be stated that to be successful an operation for ulcer must reduce permanently and in sufficient degree the acid-pepsin secretions of the stomach. This can be done by removing from four-fifths to nine-tenths of the distal portion of the stomach, leaving only a small portion of the fundus to be attached either to the duodenum or jejunum according to the surgeon's preference. Unfortunately, in solving the problem of recurrent ulceration in this manner another problem was created. Removing so great a portion of such a vital organ as the stomach resulted in a large increase in distressing postprandial symptoms and disturbances of nutrition. The dumping syndrome and inability to regain lost weight became the new problems demanding solution.

Many years ago Pavlow demonstrated that psychic stimulation of gastric secretion was passed on to the gastric glands by way of the vagus nerves. About eleven years ago Dragstedt[9] introduced and popularized sectioning of the vagus nerves as a means of reducing gastric secretion. It was soon discovered that resulting disturbances in gastric motility required an additional operation for drainage of the stomach, and so pyloroplasties and gastroenterostomy again came into vogue. Time and experience began to play their role and it was found that patients so treated were not entirely freed from the hazard of recurrent ulceration. Furthermore, the dumping syndrome occurred with about the same frequency as it did in high gastric resections. Although still advocated as a primary procedure by Dragstedt and others, most surgeons now use vagotomy as an ancillary measure combined with some type of gastric resection. This is being employed routinely by some surgeons and by others only under exceptional circumstances.

In 1906 Edkins[11] demonstrated the hormone, gastrin, secreted by the antrum of the stomach. The secretion of this hormone is initiated by the entrance of food into the antrum and then it goes by way of the blood stream and stimulates the secretion of the acid-pepsin cells. Dragstedt[10] and his co-workers have recently confirmed the presence and action of this hormone. Knowingly or unknowingly, the elimination of gastrin was the basis on which the early antral resections were performed. That this did not adequately control the excess acid-pepsin secretion has already been told.

Quite recently another method of hormonal

control of gastric secretion has been demonstrated, namely, the adrenocorticotropic factor (Bloomfield[2]). This may account for the increases in gastric secretion which sometimes occur after vagotomy.

Returning now to the distressing postprandial symptoms which frequently accompany both high gastric resection and vagotomy, while the exact causes and mechanisms of the dumping syndrome are not fully understood, experience has shown that removal of the greater portion of the stomach and disturbances in innervation must be important factors in its production. They must also be among the reasons why some patients become distressingly thin and are unable to gain weight after surgery.

A summary of the main points made thus far should be helpful here. Excess of acid-pepsin secretion is an important cause of peptic ulcer. Adequate and permanent reduction of this secretion will cure ulcers and prevent the occurrence of secondary ulcers. This can be accomplished surgically by removing the greater portion of the stomach including the antrum and pylorus. Such a procedure often results in permanent disturbances of nutrition and weight loss. Vagotomy does not prevent all recurrences and is also followed in many cases by the dumping syndrome. This is true regardless of the type of ancillary operation performed.

In 1929 Connell[4] introduced a new concept in the principle of surgical treatment of ulcer. Accepting the importance of the acid-pepsin factor in the production of ulcer, he recommended removing a large portion of the acid-secreting area and at the same time retaining the alkaline-secreting antrum and the pyloric sphincter. He did this by making a wedge-shaped excision of the body of the stomach with the apex of the wedge close to the lesser curvature but not dividing it. Connell's paper is a classic on this subject and has not received the attention it deserves.

More recently Wangensteen[25] has adopted Connell's concept of the desirability of removing the acid-secreting area of the stomach and leaving the gastrin-secreting area. At first he did this by an extension of the old sleeve resection of Mikulicz. Now he advocates leaving the lesser curvature intact and removing a large part of the body of the stomach. This is a more extensive operation performed on the same principle as Connell's.

Connell's and Wangensteen's operations have not been accepted by the surgical profession even though their results have been good. Numbers and time have not yet proved them superior to more orthodox methods of resection.

Vast clinical experience has amply demonstrated that leaving even a small part of the antrum *in situ* will result in secondary ulceration. Laboratory experiments confirm this. Some may argue that if the source of acid-pepsin secretion is eliminated this will not occur. This has not been proved. On the basis of past experience and the results of experiments it is evident that a satisfactory gastric resection performed for ulcer should remove the antrum of the stomach and a large part of the acid-secreting area of the stomach. Of equal importance, a residual gastric pouch of sufficient size must be left in order to carry on its essential functions.

It has long been known that most of the acid-pepsin secreting cells are in the body of the stomach along the greater curvature. It would seem obvious that to reduce the acid secretion and at the same time save as much stomach as possible more of the greater curvature should be removed and as much of the lesser curvature as possible be saved. Zollinger[27] in 1940 was the first to apply this principle in conjunction with antral resection. He performed this operation upon two patients with jejunal ulcers. In spite of the logic of his own deductions he has published nothing further regarding it.

No sooner had the basic principles of gastric resection and reanastomosis been established by Billroth when other surgeons began making a bewildering succession of alterations and changes in the operation. Every conceivable type of excision and anastomosis was tried. Nothing would be gained by attempting even a partial history of the various operations.

The most popular methods of resection today are the Billroth I operation and the Polya[19] and Hofmeister-Finsterer modifications of the Billroth II procedure. In the Polya operation the whole circumference of the stomach is used in the jejunal anastomosis; in the Hofmeister-Finsterer operation a large part of the lesser curvature is excised and closed and the anastomosis made adjacent to the greater curvature. Hemigastrectomy plus vagotomy is also widely done. This is in recognition of the need for preserving an adequate gastric pouch.

Cox[5–7] has made detailed pathologic and anatomic studies of postmortem specimens of

normal stomachs and those of patients with peptic ulcers. He dissects the mucosal secreting tissue of the stomach from the muscle layers and stretches it sufficiently to eliminate the folds. Cox finds that the total secreting area is greater by approximately one-third in specimens with duodenal ulcer than in those without ulcer. This variation in area of secreting surface is not directly proportional to the outside measurements of the empty stomach. Cox also made careful counts of the number of acid-secreting cells and their location. In normal stomachs there are an average of one billion acid cells, while in specimens with duodenal ulcer the number of acid-secreting cells averages nearly two billion cells. Cox finds the pepsin-secreting cells increased proportionately, but because of their structural arrangement they are more difficult to count. The acid-secreting cells and the corresponding pepsin-secreting cells lie mainly in the body of the stomach and are in heaviest concentration in the distal half of the body adjacent to the greater curvature. Here there are 30 per cent more acid-secreting cells in a given mucosal area than there are in a corresponding area in the lesser curvature. Furthermore, the much larger and irregular folds present on the greater curvature greatly increase the total secreting surface of this portion of the stomach as compared with that of the lesser curvature. These findings are of value to the surgeon who is seeking to remove the largest part of the acid-secreting area of the stomach while at the same time saving as large a gastric remnant as possible. Removing the greater curvature rather than the lesser curvature accomplishes this. The lesser curvature is the main pathway and distribution point of the external nerve and motor mechanism of the stomach. Leaving this largely intact results in a better functioning gastric pouch.

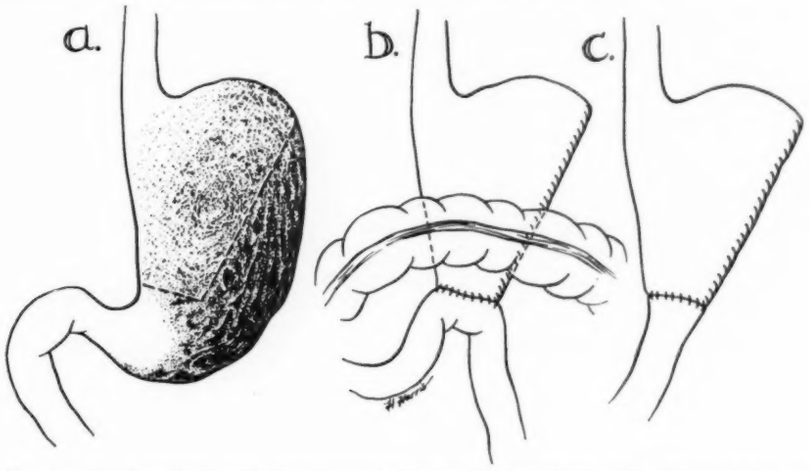


FIG. 1. A, location and concentration of acid-secreting cells; B, excision of greater curvature and Billroth II anastomosis; C, excision of greater curvature and Billroth I anastomosis.

Cox does not find a corresponding increase in mucosal area or increased number of acid-secreting cells in cases of gastric ulcer. This may be due in part to scar tissue contraction but also points to some fundamental differences between gastric ulcers and duodenal ulcers. Judd in his surgical clinics used to point out that gastric ulcer and duodenal ulcer often differed in their clinical picture and should be considered as different diseases. The possibility of cancer in gastric ulcer must always be considered. Acid volume and values are often lower in benign gastric ulcer than in duodenal ulcer. Excision of gastric ulcer and gastroenterostomy were rarely, if ever, followed by jejunal ulceration. Gastroenterostomy for duodenal ulcer resulted in a high percentage of jejunal ulcers. Dragstedt quite recently offered experimental evidence that gastric ulcer and duodenal ulcer differ somewhat in their mode of origin. Subtotal gastric resection is, however, the operation of choice in gastric ulcer as well as in duodenal ulcer.

On the basis of Cox's work we have been resecting a larger portion of the greater curvature while retaining more of the lesser curvature.[17,18] A brief description of this method follows. (Fig. 1.) The lesser curvature is freed to just above the angle of the stomach and a clamp is placed at right angles to the lesser

curvature to include a sufficient amount of the stomach for satisfactory anastomosis. A second clamp is then applied at an angle along the greater curvature so as to remove the desired amount of this part of the stomach. The portion of stomach included in this clamp is then closed and the anastomosis made to the stomach adjacent to the lesser curvature as a Billroth II procedure. In excising much of the greater curvature, a large part of the acid-pepsin secreting area of the stomach is removed. The type of reanastomosis which is made may be left to the preference of the surgeon. In most of our patients we have done a short loop, retrocolic Billroth II anastomosis. However, we have also performed Billroth I operations, especially in gastric ulcers, and have added vagotomy in a few complicated cases when this seemed indicated.

## CONCLUSIONS

In the light of past experience it is apparent that subtotal gastric resection for peptic ulcer should accomplish two things: (1) acid-pepsin gastric secretion must be reduced sufficiently and permanently, and (2) an adequate gastric pouch must be retained. The most direct approach toward accomplishing these aims is to remove that portion of the stomach which contains most of the acid-pepsin secreting cells and retain that portion where these cells are few in number. As most of the cells in question are in the body of the stomach along the greater curvature, the logic of removing this portion of the stomach seems obvious. Experience has shown also the necessity of removing the gastrin-secreting area. An operation which accomplishes these aims is described. Although time and numbers are not sufficient to draw final conclusions, we are well satisfied with the basic soundness of the method and with our results.

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# Rhabdomyoma of Skeletal Muscle

## REPORT OF A CASE

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BENIGN rhabdomyoma of skeletal muscle is exceedingly rare. Although the term rhabdomyoma is often referred to in the literature, no case reports of these tumors could be located. Tumors of skeletal muscle have been reported under the general classifications of myoblastoma (benign and malignant) and rhabdomyosarcoma. We are reporting a case that meets all of the criteria for a rhabdomyoma.

Considerable confusion exists regarding the terminology of certain neoplasms arising in striated muscle that lack unequivocal cross striations. Such tumors are usually classified as myoblastomas.[1,2,6,7,9,12,24] The term myoblastoma has unfortunately been used also to designate tumors with similar morphologic appearances arising from the tongue, skin, breast, subcutis, maxilla, vocal cord, lips, external auditory canal, trachea and bronchi, vulva and other widely varied sites.[15,20] The origin of myoblastomas has been attributed to retained or misplaced primitive myoblasts,[18] primitive muscle cells which develop in an attempt to repair a degenerative process following injury,[1] the results of a degenerative process in skeletal muscle,[13] storage cell tumors,[27] neurogenic elements,[11] fibroblastic elements[22] and skeletal muscle.[21,23] Several authors[11,13,28] have proposed that the term myoblastoma be dropped since the nature of most tumors so designated has not been proved.

The terms rhabdomyoma and rhabdomyosarcoma should suffice for tumors truly taking origin in skeletal muscle. Rhabdomyoma is a benign, true tumor in which cross striation can be demonstrated and which arises in or from striated muscle.[4,5,8,10,16,19,28] The majority of tumors of skeletal muscle are malignant.[3] Their extremely malignant nature was demonstrated in a review in 1946 in which only four symptom-free, five-year survivals were reported among 121 cases recorded in the literature.[25]

It has been questioned whether or not any of the striated muscle cell tumors of skeletal muscle can be considered benign.[21,26] It is because of this question that the following case is reported.

### CASE REPORT

A seventy-four year old white man entered the Stanford-Lane Hospital because of difficulty in swallowing of six to seven years' duration. He had had a mass on the left side of the neck since youth and had been slightly hoarse since fifteen years of age. Twenty years before, while in another hospital for an injured hand, a biopsy had been taken of the mass in his neck. This had been reported to be a benign tumor, probably a thymoma. During the past six years he had had a chronic cough which had become aggravated as his hoarseness and dysphagia increased. No history of trauma could be elicited. The patient was a fairly alert and moderately well preserved elderly man with a very raspy voice. A 3 cm. old surgical scar was present on the left anterolateral aspect of the neck at the level of the thyroid cartilage. Inferior and projecting up under the scar was a firm, non-tender mass 5 cm. in diameter. The mass appeared to arise from the upper left lobe of the thyroid gland and markedly displaced the thyroid cartilage to the right. No cervical lymph nodes were palpable. It was impossible to see the vocal cords by indirect or direct laryngoscopy because of the marked displacement of the thyroid cartilage. X-rays of the neck (Fig. 1) disclosed a large mass displacing the trachea and esophagus to the right.

* Boyd Foundation Fellow in Thoracic Surgery.

FIG. 1. Esophagram of the cervical region shows a large mass displacing the trachea and the esophagus to the right.

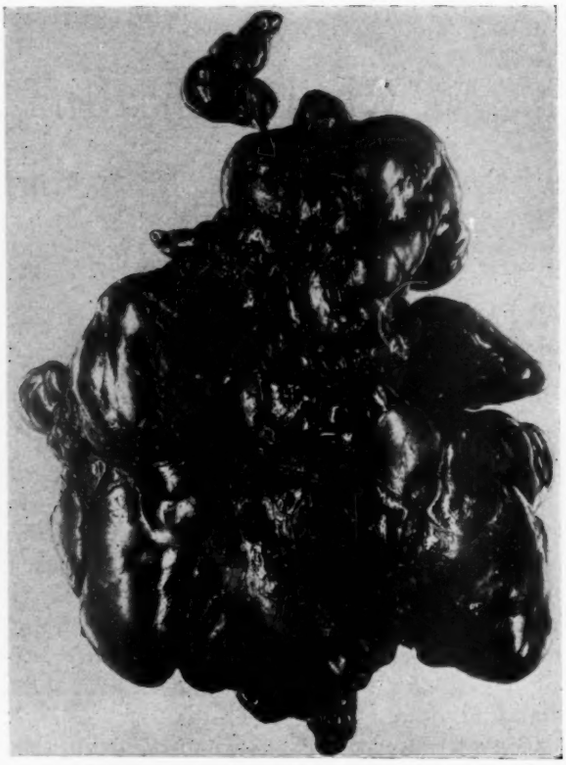


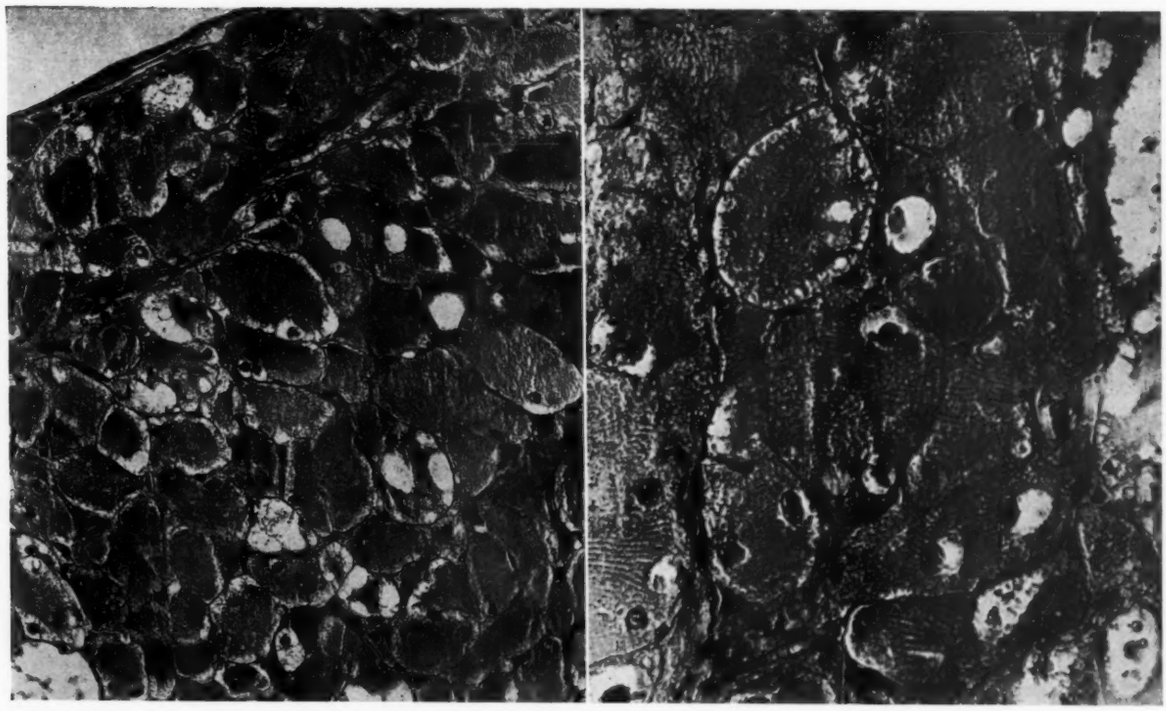
FIG. 2. The gross specimen is a 10 by 6 by 3 cm., lobulated, pink mass covered by a thin capsule.

The patient was operated upon through the usual transverse, collar-type skin incision 3 cm. above the suprasternal notch. Both lobes of the thyroid gland were small and appeared normal. The tumor lay within the thinned sternohyoid muscle, the fibers of which intermingled with the tumor. There was no evidence of invasion of the thyroid cartilage, other muscles or glandular tissue. A prominent vascular supply was present. The tumor mass was enclosed within its own thin capsule. (Fig. 2.) The mass extended from the level of the insertion of the sternothyroid muscle below to 2 cm. above the hypoglossal nerve. Anteriorly, the mass projected to the middle of the thyroid cartilage and lay upon that structure. The sheath of the carotid artery formed the lateral border. The tumor was readily dissected, with no evidence of invasion. After removal the thyroid cartilage, the greater cornu of the hyoid bone, the hypoglossal nerve, the carotid sheath and the constrictor muscles of the hypopharynx were visualized. The postoperative course was uneventful. The patient has been followed up in the outpatient clinic for fourteen months without evidence of recurrence of the tumor.

The pathologic report revealed the following: The gross specimen was a 10 by 6 by 3 cm. lobulated pink mass covered by a thin capsule. The lobules, which were loosely held together by a thin, fibrous septum, averaged about 0.5 by 1 by 1.5 cm. in diameter. The slides of the original biopsy in 1934 were reviewed. The sections of the original biopsy and the specimen looked exactly alike. The entire mass was made up of large, pale cells with abundant granular cytoplasm. The small oval nuclei were placed peripherally in the cells. Two or more nuclei were often present in a cell. The groups of cells were separated by a thin, fibrous septum and each cell was surrounded by a fine reticulum network. (Fig. 3.) Occasional cells showed cross striations. Some cells showed distinct cross striations and granules in the same cell. (Fig. 4.) There was a thin, fibrous capsule around the tumor. The pathologic diagnosis was rhabdomyoma.

## COMMENTS

A case of a skeletal muscle tumor of the neck in a seventy-four year old man has been reported. The tumor had been present for more than fifty-five years and was recently removed because of local pressure symptoms. Twenty years before, a biopsy taken at an outside hospital had disclosed a benign tumor, probably a thymoma. Review of these slides



3 4

FIG. 3. Photomicrograph showing thin, fibrous capsule, fibrous trabeculae and granular cells. × 220.

FIG. 4. Photomicrograph showing cross striations and granules in the tumor cells. Hematoxylin and eosin, × 440.

disclosed a tumor which was morphologically identical to the one removed at the present admission. The tumor was composed of large, irregular-sized tumor cells with frequently multiple non-centric nuclei and granular cytoplasm which commonly exhibited cross striations. Mitotic figures were not seen. The tumor was enclosed in a capsule and no evidence of invasion was found.

This tumor matches the description of some of the granular cell myoblastomas reported in the literature. Some authors[14,17] have expressed the opinion that the granular cells and the striated cells are distinct from each other. Klemperer[17] found no cells with both striations and granules, but Horn and Stout[14] show one picture of cross striations and granules in the same cell. That the granular cells and striated cells in our case are the same cell is shown by the two observations that: (1) the striated cells are morphologically identical to the granular cells and occur diffusely among the latter, and (2) there are occasional cells with both distinct granules and cross striations. Since the granular cells are definitely a part of the benign striated muscle tumor, we believe this tumor should be called rhabdomyoma to separate it from the heterogenous group of tumors of unknown origin which are included under the title of granular cell myoblastomas. All tumors which show definite cross striations in the cells and arise from skeletal muscle should be classified as rhabdomyoma if benign and rhabdomyosarcoma if malignant.

## SUMMARY

Benign rhabdomyoma of skeletal muscle is exceedingly rare. No recorded cases could be found in the medical literature.

A case is reported that meets all of the criteria of a benign rhabdomyoma: The tumor (1) is of long duration (fifty-five years by history and twenty years by microscopic examination) without evidence of malignancy; (2) arises directly from the skeletal muscle of the neck; (3) contains numerous cells showing cross striation; (4) has an intact capsule without evidence of invasion; (5) shows no microscopic evidence of malignancy; and (6) shows no evidence of recurrence fourteen months after surgical extirpation.

Evidence is presented to show that the granular cells in this type of tumor are the same as the cells containing cross striations. Reasons are presented to show why this type of tumor should be called a rhabdomyoma and not a granular cell myoblastoma.

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# End Result of Using Vitallium Tubes in Common Duct Strictures

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ANY surgeon who has experienced the difficulties of treating injuries of the common bile duct is well aware of their tendency to result in stricture formation. Once a stricture of the common duct occurs, it may be progressive, persistent and result in cholangitis with liver damage.[14] Most of these injuries are accidental and occur during cholecystectomy. As Sir James Walton[18] has said: "Every removal of a gallbladder, easy though it may seem, is fraught with very great danger, and one small error may convert a patient with a mild disability into one in immediate danger of death or of prolonged misery, and many operations, which at best may only give an incomplete life."

The best course is to avoid injury of the common duct, for once it is damaged the skill and ingenuity of the best of surgeons may fail to restore the patient to health and useful living.

Many methods have been tried to cure benign strictures of the common bile duct. Dilatation, fistula reimplantation, the Wilms-Sullivan operation and tubular grafts have all failed. The procedures most commonly used are: (1) hepaticoduodenostomy;[10,16,17] (2) Roux-Y anastomosis of jejunum to duct;[5,6,15] (3) end-to-end anastomosis over a rubber T-tube or (4) over a Vitallium® tube.[11–13]

End-to-end anastomosis after removal of the damaged area is the most physiologic procedure for it restores the normal anatomic relations and preserves the function of the sphincter of Oddi. It is most apt to be successful when a mucosa-to-mucosa suture is used, when tension which might separate the duct ends before healing is avoided, and when the anastomosis is held open by a tubular splint until the scar tissue loses its tendency to contract. How long this takes is not known but it is probably nine to twelve months.

The tube which is left in the bile duct to hold open the end-to-end anastomosis has been made of rubber, Vitallium, "bouncing clay" tantalum and polythene. Each has its disadvantages. I agree with Cattell[4] when he says that "the type of material over which the repair is performed is not as important as the way the procedure is carried out." Dissatisfaction with the tissue irritation and fibrosis occasionally caused by rubber led me[11] to use a tube of Vitallium. It was selected because of its lack of tissue reaction, its smooth surface which did not attract concretions, and its high tensile strength which permitted a thin wall with a maximum lumen for its external diameter. Tantalum also has these characteristics and is more malleable but it cannot be welded, so no anchoring flange can be attached to it. Plastics were discarded because most of them cause tissue irritation. Non-irritating polythene has not been made in the shape of a T-tube because of the inability to make this shape in one piece.

Vitallium tubes have the disadvantage of being so hard that they cannot be altered at the time of operation nor can they be removed except by an operation.

The first insertion of a Vitallium tube was performed on February 26, 1940. Recently this patient returned with symptoms of common duct obstruction. At reoperation* on December 5, 1952, a tube plugged with black concretions (Fig. 1) which was lying free in a dilated duct was removed. This case was previously reported in detail fourteen years ago.[11] It is recorded here briefly to illustrate the follow-up and eventual result for it is quite typical of others.

## CASE REPORT

M. T. (No. 151537) was a thirty year old mother of five children when admitted on March 29, 1939.

* Performed by Dr. Harry D. Kingsley.

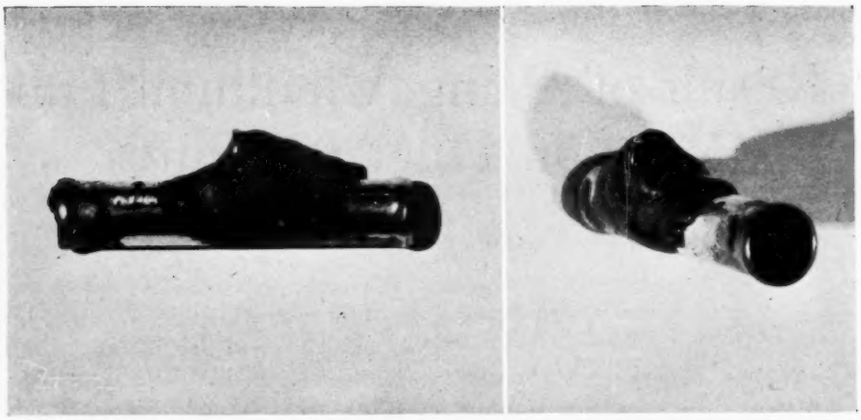

FIG. 1. Side and end views of a plugged Vitallium tube that was removed twelve years after its insertion. The tube was lying free in the common duct and had given symptoms for only a few months.

First operation (July, 1937): The patient had had a cholecystectomy elsewhere. She was told that the common duct contained several stones which were removed. Recovery was slow with drainage from the wound so she was in the hospital five weeks. Soon after the wound healed she began having attacks of epigastric pain associated with nausea, vomiting, chills, fever and jaundice.

Second operation (May, 1938): This had been done elsewhere, at which time the patient was told a stone was removed from the common duct. A catheter drained bile after this operation and she felt perfectly well until it was removed, when the symptoms of pain, nausea, vomiting, chills, fever and jaundice returned.

On admission to this hospital she was found to be chronically ill with sallow skin, icteric scleras, healed abdominal scars and enlarged liver. Except for slight elevation of the icterus index, the laboratory findings were normal. A diagnosis was made of stricture of the common duct with cholangitis.

Third operation (April 5, 1939): After release of many adhesions, dissection in the scar tissue about the gastrohepatic ligament revealed a 1½ inch, thread-like stricture of the common duct. The hepatic duct above was dilated, contained bile under pressure and two stones. A stump of the common duct protruded about ¼ inch above the pancreas. The stricture was excised and an end-to-end anastomosis done over a T-tube.

On May 18, 1939, six weeks after operation, a cholangiogram was taken which showed a patent anastomosis so the T-tube was removed. In retrospect it should have been left in longer, for within three months she was again having attacks of cholangitis. At this time it was discovered she was pregnant; and after treatment failed to influence her symptoms, the pregnancy was interrupted for it was a menace to her.

The cholangitis grew worse until she was having a daily chill with fever to 40°C. (104°F). It was apparent that she could not survive for long, yet it was thought that there was too little duct left for another plastic repair. It was decided that if a non-irritating, rigid tube could be inserted in the strictured area, it would hold it open enough to allow adequate drainage. A Vitallium tube was designed and made for me by Austenal Laboratories, New York, N. Y.

Fourth operation (February 26, 1940): After freeing dense adhesions the dilated stump of the hepatic duct was isolated and a stricture found at the site of the former anastomosis. There was a stone above the stricture. It was removed and the Vitallium tube was inserted so that its ends were in the patent duct above and below the strictured area.

The result was dramatic. The patient lost her symptoms of cholangitis and regained her strength and vitality so that she was restored to a life of useful living from one of chronic invalidism. In fact, she did more than the usual mother of five. During World War II she worked in a war plant and later acted as a supervisor in a department store during the week and as a hostess in an inn on Sundays. It is pertinent to note that sodium taurocholate had to be discontinued because of indigestion and diarrhea.

She was well until January, 1952, when she began to have some upper abdominal distress. In September, 1952, she had a bout of cholangitis, the first in twelve years. It was followed by two other attacks the following month. She was seen on November 20, 1952, with a history that in the last attack (five weeks before) she had had subcostal and subscapular pain, nausea, vomiting, chills, fever and jaundice. She was told that in all probability the Vitallium tube had plugged and should be removed. An x-ray of the abdomen showed the tube in its usual location.

Fifth operation (December 5, 1952): My associate, Dr. Harry D. Kingsley, exposed the common duct which was found to be dilated to over 1.5 cm. in diameter. A small incision was made in it and the plugged tube (Fig. 1), which was free in the lumen, was removed. There was no constriction of the duct, the mucosa was smooth and normal in appearance, so the duct was closed with interrupted silk sutures and the abdomen drained with a cigarette drain in the subhepatic space.

There was slight superficial infection in the lower angle of the wound (culture of bile showed Escherichia coli). The patient was discharged December 16, 1952, on her eleventh postoperative day.

She returned on February 15, 1953, with an attack of pain, chills and fever but no jaundice. This was interpreted as being residual liver infection. She has been well since that time.

In 1946 a follow-up study[13] was made, five years after the publication of the method. At this time it was found that 11.3 per cent of the cases had difficulty from plugging of the tube. The sediment which plugged the tubes was analyzed on three occasions with the following results:

| | |
|---|---|
| January 21, 1944: | |
| Lipids | 0.1664 gm. (38 per cent) |
| Insoluble | 0.2655 gm. |
| March 24, 1945: | |
| Lipids | 0.1619 gm. (36 per cent) |
| Insoluble | 0.2881 gm. |
| October 23, 1945: | |
| Lipids | 0.146 gm. (56 per cent) |
| Insoluble | 0.114 gm. |

It is assumed that the lipids are largely cholesterol. Only from 0.0015 gm. to 0.0075 gm. of calcium could be extracted from the insoluble fraction so the remainder is presumed to be bile pigment. This is disappointing for only the cholesterol can be influenced by such medication as sodium taurocholate or sodium dihydrocholate, as shown by the work of Best and his co-workers.[1,2] However, these drugs are of value[7] not only in preventing concretions from forming on the tube but also in apparently removing them when formed. At least we have had patients with beginning symptoms of biliary obstruction and mild jaundice who have been relieved by giving hydrocholeretics. It was assumed that they had begun to plug their tube and that the drug dissolved the cholesterol fraction which released the sediment to reopen the lumen.

In 1946 two cases (No. 171848 and No. 186570) were reported.[13] These patients were cured by removal of a plugged Vitallium tube and closure of the incision in the common duct. Only the subhepatic space was drained; no tube was left in the duct. The tubes plugged in two and three and a half years, respectively, but in both instances the stricture was cured; the duct was lined with smooth, velvety mucosa and its lumen was of normal caliber. This experience was repeated by Dr. H. D. Kingsley, when on three occasions he removed plugged tubes that we had inserted. One of these was the case herein reported and the other two patients were B. G. (No. 221606) and J. P. (No. 330882). All are well. From this one may conclude that if a Vitallium tube holds open a strictured common duct for over a year it may be removed with impunity, for by this time the tendency to reformation of stricture has ceased.

This happy outcome may not occur if the duct is manipulated and drained with a rubber T-tube at the time of removal of the plugged Vitallium tube. At least in two cases, one here (M. P., No. 360447) and one elsewhere, recurrent difficulty followed such a procedure.

Walters[17] has said, "No matter whether the tube used as a splint is made of natural or synthetic rubber, polyvinal material or Vitallium, if it is left within the duct long enough bile pigment will accumulate in its lumen and around its sides and varying degrees of obstruction and infection will be produced. The tube will then have to be removed." I agree with this statement as a true generalization. The patient reported herein had a free interval of twelve years but in the end the tube plugged. So, unfortunately, it must be assumed that if a tube of any kind is put into the common bile duct, sooner or later it must be removed.

Another complication in the use of Vitallium tubes, even in end-to-end anastomosis, has been their passage out of the duct into the intestinal tract. This would not be surprising in any type of duct-intestinal anastomosis for it is nearly impossible to prevent the passage of any type of tube in these cases. However, surgeons have told me of tubes that have passed from the common bile duct through the sphincter of Oddi and into the intestine. Thus the anchor flange on these tubes is not a certain method of stabilization.

## COMMENTS

The results reported for the treatment of common duct strictures by hepaticoduodenostomy or Roux-Y anastomosis are practically as good as those for end-to-end anastomosis. However, there is much to be said for restoration of the anatomic continuity of the duct by anastomosis. With perfection of technic it should give the best results for it recreates a normal physiologic mechanism. However, one of its technical necessities is the prolonged use of an indwelling tube. So far the perfect tube for this purpose has not been devised, although both a rubber T-tube and a Vitallium tube have been useful. The ideal common duct tube would have the following characteristics: (1) A maximum lumen with a minimum thickness of wall for in some scarred, rigid ducts only a small diameter tube can be inserted. (2) It should be strong enough to avoid breaking, rigid enough to prevent kinking, flexible enough to conform to the duct and soft enough to cut to length at operation. (3) It should not cause tissue reaction which would lead to fibroplasia and reformation of stricture. (4) It should not deteriorate when left in the duct for over a year. (5) Its walls should be smooth to minimize concretion formation and plugging of the tube. (6) It should have positive stability to avoid its passing out of the duct. (7) It should be removable when no longer needed.

It may never be possible to devise a common duct tube which meets all these requirements but it should be possible to attain many of them. If this is done, the results from end-to-end anastomosis of the common duct for treatment of stricture would be further improved.

## SUMMARY

1. A follow-up is reported on the first case in which a Vitallium tube was used for repair of a stricture of the common bile duct. This patient had complete relief of symptoms for twelve years after which the tube plugged. At the time of its removal the stricture was cured and the patient has been well for two years since this operation.

2. Four other cases are mentioned in which the damaged duct was restored to normal over a Vitallium tube in periods ranging from one and a half to three years when these tubes plugged. Removal of the plugged tube and suture of the opening in the duct resulted in permanent cure.

3. Two cases are mentioned in which other surgeons manipulated the duct and inserted a rubber T-tube at the time of removal of a plugged Vitallium tube with recurrence of symptoms after the T-tube was removed.

4. It is probable that a tube of any material yet devised will plug if left long enough in the common bile duct. This result is retarded or minimized by the use of hydrocholeretic drugs.

5. The characteristics of the ideal tube for prolonged implantation in the common duct are enumerated. Thus far this ideal has not been attained so the best results from end-to-end anastomosis, which restores the normal anatomic relationship, have not been realized. There is still room for improvement.

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# Vascular Replacements and Reconstruction Utilizing Inert Material

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IT has been demonstrated that when segments of arteries are replaced by arterial homografts or heterografts the implanted tissues serve essentially as a scaffolding material and are eventually replaced by the tissues of the recipient. These replacing tissues consist essentially of fibrous tissue with a glistening inner lining which closely resembles the endothelial lining of the adjacent artery of the host.

If an inert material could be substituted for the homografts, which are scarce and difficult to collect and preserve sterile, the technic would be greatly simplified and could be applied much more widely.

Hufnagel used impervious, semi-rigid and rigid plastic tubes, and found they would serve as a conduit for the blood, became lined with an intima-like membrane and not become occluded with clot in the immediate postoperative period.

Blakemore and Voorhees[1] used tubes constructed of woven Vinyon N fibers, an inert plastic material.

Two recent pertinent and fundamental observations have been made repeatedly which should greatly influence vascular surgery. First, the diseased intima can be stripped out of an artery to re-establish blood flow through the vessel without the entire lumen becoming occluded immediately by a blood clot when circulation is re-established. Second, whenever a homograft or heterograft is implanted to replace a segment of artery, the tissue of the graft acts simply as a scaffolding and is eventually replaced by ingrowth of the tissues of the host.

Since the tissues of a homograft or heterograft are replaced by fibrous tissue and collagen fibers, it would not be expected that this tissue will permanently withstand arterial blood pressure without dilatation of the implanted segment. On the other hand, it is surprising how well these segments have actually held up, as has been demonstrated by Gross, with implants for correction of coarctation of the thoracic aorta which have been in place for five years without appreciable dilatation. It is true that the number of cases is small and may well fail to indicate the number of failures in the future.

Since these facts pertain it would seem logical to expect that a tube made of a pervious, woven, inert material would serve favorably as an implant for replacement of defects in the arterial bed. It was reasoned that multiple layers of woven, inert, plastic material would serve as a scaffolding into which an enmeshed fibrinous clot would become invaded by fibroblasts and capillary buds. The fibroblasts would lay down fibrous tissue, collagen fibers would be deposited and the whole would be vascularized by capillary ingrowths. Voorhees, Jaretzki and Blakemore,[6] and Blakemore and Voorhees[1] fashioned single-layer tubes from a woven plastic material, Vinyon N, and used them as arterial prostheses. They found that the interstices of the material were rapidly sealed by fibrin and enmeshed blood cells only to be invaded by fibroblasts coincidentally with the deposition of longitudinally oriented collagen fibers. This process is completed in about four weeks and includes the innermost fibrinous layer which, in turn, is further covered by fine granulation tissue. This granulating surface shows flattened islands with a smooth greyish appearance in about seven weeks. These islands become confluent by the fourteenth week and the smooth surface is identical with the endothelial lining of the adjoined artery.

Sawyer and Pate[3] demonstrated that heparinized blood will clot at the positive pole when a current is passed through two immersed

platinum electrodes of an electrolytic cell. Sawyer, Pate and Weldon[4] showed that the intima of a normal uninjured artery is negatively charged as compared with its adventitia. A crushing injury will reverse this charge and the polarity of the intima becomes positive with respect to the adventitia. Minor injuries or careful dissection to free a vessel from surrounding tissues will, however, cause the intima to become more negative with respect to the adventitia. The intima of fresh grafts immediately following transplantation are positively charged with respect to the adventitia and a crush injury will increase this difference of potential.

Further observations by Sawyer and Pate[5] on freeze-dried grafts did not exhibit any potential difference between the intima and adventitia nor did crush injury of a reconstituted freeze-dried graft result in a potential difference. A transplanted freeze-dried graft generates no potential difference, but the negative potential in the adjoining recipient artery is increased immediately and may rise as high as four to ten times normal levels in the course of two to four days and return to normal as healing proceeds.

These observations would indicate little tendency for a freeze-dried graft to clot insofar as this process is influenced by electrical potentials. The inner surface of a freeze-dried graft develops a negative charge about fourteen days after implantation.

Although no actual measurements have been made on inert pervious tubes implanted into arteries, it can be anticipated that they will follow the pattern of the dead, freeze-dried graft. Furthermore, it can be expected that standing blood will clot rapidly in either a freeze-dried graft or an inert tube. Wherein lies the difference when the blood is streaming?

We have observed that a pervious, inert tube made of raw nylon forms a clot within the meshes of the tube and also on its inner surface. It is known from the hydrodynamics of the flow of liquids through a tube that the rate of flow is maximal at the center and minimal at the outer layer in contact with the wall of the tube. At the outermost layer the fluid is at a virtual standstill. Therefore, in our highly specialized system the blood would be at a standstill in the zone of contact between the streaming blood and the inner thin layer of clot, and should proceed to coagulate and completely occlude the tube. This does not occur. It can be shown that the streaming blood is not in direct contact with the inner layers of clot. The inner surface of this clot is covered rapidly with a mosaic of polymorphonuclear leukocytes. These leukocytes form a cellular barrier between the inner surface of the clot and stagnant or slowly moving outer core of the streaming blood.

While this cellular layer forms an effective barrier and prevents clotting, it probably does not act as a biologic membrane and develop a membrane potential. In all probability there will be little difference in the response when any one of the several inert plastic materials—Vinyon N, nylon, orlon, dacron or others—is used to construct the tubular implant.

## EXPERIMENTAL OBSERVATIONS

*Materials and Methods.* Prostheses were constructed primarily from raw nylon. The final prosthesis consisted of two parts; an inner liner of 70 denier, 76 by 106, unfinished nylon taffeta covered by one to three layers of tricot weave of unfinished nylon. The inner liners were tailored accurately to the actual measurement of the vessels to be replaced both as regards diameter and length. The frame on which the tubes are constructed is shown in Figure 1. The design of this frame permits the prosthesis to be made with a tapering diameter. The prostheses can be constructed in a few minutes at the operating table. (Fig. 1.) This same holding frame is used in constructing bifurcating prostheses.

The inner liner of the prosthesis is sutured in place as indicated in Figure 2. If blood under full arterial pressure is released into the implant, bleeding through the material is brisk. This leakage ceases in the dog in one to three minutes and in the human in three to five minutes.

The blood loss can be reduced to a few milliliters if the implant is moistened with a small quantity of blood which is permitted to clot in the meshes of the cloth before re-establishing full arterial pressure. A dry gauze sponge is placed beneath the implant before it is moistened to absorb the excess of blood and thereby avoid the formation of a clot in the dependent side of the lumen of the tube. The suture lines are sealed effectively if they are rolled gently under the thumb and forefinger just as is practiced in any vascular suture. As an addi-

tional precaution in the case of the human subject, a sheet of rubber tissue should be passed beneath the implant and cupped up around it to form a reservoir prior to release of the distal clamp. If excessive bleeding occurs, the blood can be sucked into a blood bottle

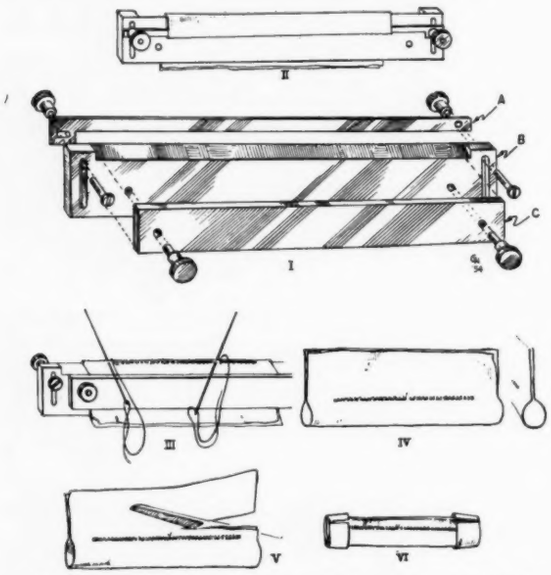


FIG. 1. Adjustable frame designed to hold the fabric from which the prosthesis is made. I, detailed view of various parts of the apparatus. A is the adjustable bar over which the fabric is folded. This bar can be placed at the desired distance from the beveled edge of B at the distance required to give the size of tube needed. If the bar is placed parallel to the beveled edge, the prosthesis will have a uniform diameter from end to end. If bar A is placed in an oblique position to the beveled edge of B, the prosthesis will taper from one end to the other. C can be clamped against B to hold the fabric in place (as indicated in II) for sewing, as illustrated in III. A running stitch begins by being tied in the center, carried to each end, then returned to the center again and tied. IV, the inner liner of the prosthesis upon removal from the frame. VI, the finished inner liner, with cuffs turned back, ready for implantation. Since the prosthesis is made in a flattened state, the measured diameter of the recipient artery is multiplied by $\frac{\pi}{2}$ or 1.5 to obtain the "flattened" dimension used in the apparatus.

containing citrate solution and be returned to the patient. As soon as the bleeding checks, the proximal clamp is released. When the blood loss has stopped, the cuffs are folded over the ends of the recipient arteries and secured with a few interrupted sutures of No. 00000 braided nylon. The reinforcing tricot weave nylon is attached to the seam of the inner liner with a few interrupted sutures of No. 00000 braided nylon. The required number of layers is wrapped around the implant and the ends of the artery and sutured in place. The ends of these reinforcing layers are sutured to the perivascular tissues to secure this fabric

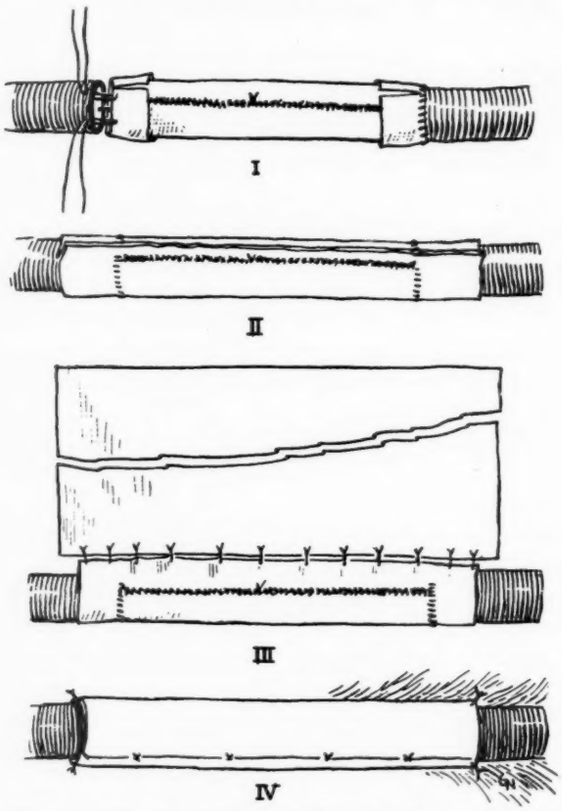


FIG. 2. The introduction of a simple prosthesis. I, one end sewed in place with continuous, over and over stitch of No. 00000 braided silk. The opposite end shows the everting, mattress traction sutures in place. II, the inner liner of 70 denier, 76 by 106 unfinished nylon in place with the cuffs extended over the lines of suture. III, the tricot weave of unfinished nylon "wrap-around" stitched to the longitudinal seam edge of the inner liner. IV, two layers of the "wrap-around" in place and stitched both longitudinally and to the perivascular tissues at both ends.

in the desired position. Anticoagulants are not used.

Once the technic has been mastered and the prostheses accurately tailored to the dimensions of the recipient arteries, there is little tendency for clotting to occur. The animals show little reaction to the procedure and return to normal activity within two or three days without any special care.

Implants have been made successfully in thirty-two adult dogs. These implants have

been recovered at varying intervals for study. Some prostheses have been removed after thirty minutes. Microscopic study was made of the surface layer of the inner fibrin clot exposed to the streaming blood. This innermost layer was observed to be composed of polymorphonuclear leukocytes. Very few lymphocytes are found in this surface layer. It is considered that this surface layer functions as a viable cellular lining of the prosthesis and prevents early clotting. In all probability any one of these leukocytes is not necessarily a permanent member of this cellular mosaic, but rather may be replaced by other leukocytes from time to time. Also, the fibrin layer covering the inner surface of the inert prosthesis tends to become thickened until it has been thoroughly infiltrated by capillary buds and the surface covered with capillary loops or granulations. Also, it is thought that the final endothelial lining of the prosthesis is influenced by the presence of these capillary loops or granulations. Endothelial proliferation is accelerated at either end and spreads along the inner surface of the granulations covering the fibrin layers.

The tissues of the host surrounding the prostheses invade the mesh of the cloth. It may be that the individual fibers of the plastic material are simply encased by the surrounding tissues of the host, but the prosthesis as a whole is not simply encapsulated as occurs when a solid, impervious tube is buried in the tissues of the host. The prosthesis is invaded by the surrounding tissue.

The new segment of vessel is essentially a tube of vascularized fibrous tissue and collagen fibers intimately intermeshed with several layers of strands of inert elastic fibers of plastic material. These elastic fibers of the plastic act to support the fibrous tissue and should prevent late dilatation of the implant subjected to long-standing arterial pressures. Multiple layers are suggested as a safeguard against rupture of a strand of a single layer of inert material with a possible resulting aneurysmal dilatation.

### GROSS AND MICROSCOPIC APPEARANCES OF IMPLANTS

*Initial Reaction.* The early changes noted in the nylon graft that replaces the wall of the aorta includes the prompt migration of plasma, red blood cells and leukocytes through the wall and into the surrounding spaces between the layers of the graft and the adjacent tissues. This sequence is followed by the formation of a thrombus. The early thrombus shows strands of fibrin which form irregular division of the erythrocytes and other blood elements from one to eighteen hours after the replacement of the segment of vessels. A layer of leukocytes is present adjacent to the luminal surface of the nylon material and covers the surface of the thrombus. Smears prepared from the superficial inner layer of the thrombus disclose the majority of these cells to be polymorphonuclear neutrophils.

*Four- to Ten-day Period.* Within four days after the replacement of the vessel there occurs a more compact arrangement of the blood cells and degenerated elements that are included in the thrombus. This arrangement is associated with dilatation and some proliferation of the small capillaries in the perivascular tissues adjacent to the outer surface of the prosthesis. Migration of fibroblasts between the bundles of nylon fibers is a conspicuous feature which is associated with a few capillary buds that are extending into this area. Leukocytes are prominent in the tissue surrounding the suture material at the site of the anastomosis. These cells are also more densely concentrated on the luminal surface of the thrombus than elsewhere. Within four to ten days this fibroblastic framework of the thrombus becomes more compact in its arrangement near the site of anastomosis and is associated with invasion of this area by capillaries. The first indication of endothelialization occurs at the site of union of the graft with the transected artery. Extensions of capillaries to a point near the luminal surface of the thrombus is noted at this stage, but definite formation of an endothelial lining of the large vascular channel cannot be traced directly to these vessels. Changes occurring in the peripheral portion of the graft at this time include the presence of numerous macrophages which contain granules of hemosiderin within their cytoplasm.

*Twenty-day Period.* The process of organization of the thrombus on the luminal surface progresses. The portions of the vessel wall which are surrounded by the cuff of plastic material that extends around the adventitia do not have as clearly defined cellular detail as the adjoining vessels. A chronic inflammatory response is present in the adjacent tissue

with fibroblastic proliferation and many lymphocytes and macrophages. Granular basophilic-staining deposits suggestive of calcification are encountered in the organizing thrombus near the network of nylon fibers close to the luminal surface. The earliest appearance of this process of calcification is seventeen days following the introduction of the prosthesis in a single instance. Sections of other vessels removed at this time interval show no evidence of deposition of calcium.

*Thirty-day Period.* Animals sacrificed at intervals of twenty-nine, thirty and thirty-four days show an organizing thrombus which projects into the luminal portion of the vascular channel. The inside diameter of the proximal and distal end of the artery at the sites surrounded by the cuffs are considerably diminished due to subintimal proliferation of connective tissue. This proliferation results in an asymmetric location of the lumen and a marked narrowing of the inside diameter. Proliferative activity occurs in the endothelial cells in this area. Distal to the anastomotic site these endothelial cells cover the organized, fibrosed luminal surface of the prosthesis for a variable distance. Near the mid-portion of this prosthesis phagocytosis of debris and fibroblastic infiltration of the thrombus still occurs. Deposits of basophilic-staining material suggestive of calcification are present at the base of the thrombus and are adjacent to the luminal surface of the inner layer of nylon material. At these points of calcification few capillaries are encountered. In the more peripheral layers of this material a foreign body type of reaction occurs.

*Forty-day Period.* Progress continues in the process of organization mentioned previously. An animal sacrificed at forty-six days shows a uniform, compact, parallel arrangement of fibroblasts on the luminal surface of the prosthesis which vary from ten to eighteen cells in thickness. The collagen fibers stain uniformly and the luminal surface is covered with a smooth, single layer of endothelial cells. Minimal inflammatory reaction is noted at the line of anastomosis. Foreign body reaction in the wall of one prosthesis is not as marked as observed in previous sections.

*Fifty- to Ninety-day Period.* The three animals studied at this interval show a progressive fibrosis of the wall of the prosthesis. Endothelialization of the luminal surface has not been completed in the one animal that has been sacrificed at the end of ninety days. Multiple foci of calcification are noted in the intimal portion of this vessel. The majority of these deposits occur near the mid-portion and at the base of the fibrous connective tissue adjacent to the inner layer of the synthetic material. Other deposits are noted between the layers of the nylon. A loose arrangement of fibrin and acidophilic-staining debris projects into the lumen of the central portion of the vessel that has not been completely lined with endothelium. Few vessels growing through the wall of the graft extend into this material on the luminal surface. Phagocytic activity occurs within the wall to a more marked degree in the mid-portion of the prosthesis.

### CASE REPORT

H. V. (Unit History No. 2804-K), a forty-nine year old Negro man, was shot in the right thigh with a charge of buckshot two years previous to admission. An arteriovenous fistula with a false aneurysm resulted in the femoral vessels distal to Hunter's canal. The artery was isolated proximally and distally. The sites for resection of the artery were determined, and the length of the resulting defect and the diameters of the artery at the levels of the resection were measured. The inner liner of the prosthesis was accurately tailored to these dimensions. The segment of artery was resected and the defect in the vein wall was sutured to reconstruct the vein. The inner liner was then sutured in place. (Fig. 2.) A long arteriosclerotic plaque occupied approximately one-third of the circumference of the distal artery and the anastomosing sutures were placed directly through this plaque. An estimated 500 cc. of blood were shed through the prosthesis when the clamp was released before it was rendered impervious by fibrin in the meshes of the fabric. The cuffs at the two extremities of the prosthesis were then turned across the suture lines and secured with a few interrupted sutures of No. 0000 nylon. A length of nylon tricot was then secured to the seam edge along the inner liner with a few No. 0000 nylon sutures and two layers of the tricot were wrapped around the inner liner and sutured with interrupted No. 0000 nylon. (Fig. 3.) The ends of this tricot covering were sutured to the perivascular tissues in order to place the material under a slight stretch. The tricot,

FIG. 3. The immediate appearance of a multilayered nylon prosthesis bridging a defect in a femoral artery.

FIG. 4. Arteriogram taken on the fourteenth postoperative day of prosthesis (extending from A to B) used to repair an arteriovenous fistula. The narrowed appearance of the recipient artery distal to B is due to the presence of a long arteriosclerotic plaque. The suture line at B passes through this arteriosclerotic thickening.

having been sterilized by autoclaving, was soaked for thirty minutes in 1 per cent neomycin solution just prior to use. The wound was washed out with 1 per cent neomycin solution and closed with interrupted nylon sutures. Clinically, the result was excellent. The right foot was slightly warmer than the left and pulsations in the dorsalis pedis artery were strong and of greater amplitude than before operation, as well as being stronger than the pulsations in the left foot. Arteriogram taken on the fourteenth postoperative day showed the lumen to be patent. (Fig. 4.)

## COMMENTS

The studies which have been outlined in this presentation, and those of other investigators, would certainly indicate the practicality of using pervious, flexible tubes tailored from inert plastic materials for replacement of segments of arteries. These prostheses serve as inert scaffolding into which viable host tissues grow. The material of the prostheses ultimately serves as reinforcing to prevent dilatation of the host tissues under the prolonged arterial pressures. The prostheses made of nylon fabric actually pulsate.

The concept of an inner liner which has been developed herein has been extended to include the use of autogenous and homogenous vein segments which serve as the inner liners. The vein is covered with a tube made of nylon taffeta to control the diameter to which the vein can be expanded by the arterial blood pressure. In this manner the size of the vein is not so important. The taffeta covering is tailored to limit the diameter to which the vein can dilate. Furthermore, under these circumstances a homograft would become acceptable because the taffeta covering would give the required supporting strength.

The observations of Parsons, Gerbode and Cox[2] that an autograft covered by silver foil receives sufficient, immediate nutrition from the streaming blood within the lumen of the transplant to support the viability of its tissues

would indicate that a venous autograft would survive when covered by a pervious sheath of an inert plastic fabric. In fact, immediately successful venous heterografts covered by inert fabrics have been accomplished and will be reported elsewhere.

This particular type of replacement would be especially indicated where relatively long segments of peripheral vessels, such as iliacs, femorals and carotids, are destroyed or must be replaced.

Study of the development and change of electrical potentials across the boundary of these inert prostheses as they become vitalized is in progress and will be reported later.

It is not our purpose at this time to draw conclusions regarding the ultimate clinical significance of these observations.

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# Atypical Neuralgias of the Head

## HEADACHES, SO-CALLED MIGRAINE AND COMPLICATIONS OF WHIPLASH INJURIES AND OTHER CERVICAL TRAUMA

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THE extracranial source of headaches is extremely common, with "migraine" occurring in about 10 per cent of all patients seen in general practice. Such intracranial disturbances as brain tumor or cerebral vascular anomalies must be considered first in any patient with headaches, and a neurologic examination with a study of the eye grounds is essential. Hypertension, renal disease and the toxicity of gastrointestinal disorders must be ruled out as well as disorders of the nasal or paranasal regions or of the eyes, teeth or ears.

When these or other possible explanations (such as sprain of the neck from whiplash injury) for the headaches have been studied and found normal, the atypical neuralgias of the head and face are considered. Pain that produces headaches can be attributed to afferent sympathetic nerve fibers in and accompanying blood vessels which may be sensitive in spots. For the same reason, it has been found that skin, subcutaneous tissue, galea, ligaments, and fascia of temporal, occipital and cervical muscles as well as the muscles themselves are sensitive to pain. All of the arteries and veins of the scalp have been found to be sensitive to pain.[1] Points of sensitization from trauma and/or toxins may cause contractions in the muscles about the head and neck, which in turn provide fresh sources of sensitized areas producing pain.

Of all neuralgic pains in the head and face, only those of a momentary paroxysmal nature can be classified as a true tic douloureux or as a neuralgia of the fifth, eighth and ninth cranial nerves. The others, including the atypical neuralgias of the head and face, migrainous headache and occipital neuralgia, are of sympathetic origin.

Adams[2] recently stated that "Pain, in its severer forms, as for example, trigeminal neuralgia, migraine, or the various colics, is one of the heaviest crosses the human race has to bear . . . Persistent pain, whether mild or severe, over weeks, months or years can produce serious and far-reaching sequelae, which affect the patients' work, play and sleep, alter personalities and produce changes in every phase of their daily lives." He went on to emphasize that "Until recent years physicians as a whole tended to minimize the importance of persistent pain, particularly if the cause was not readily apparent." He, like former authors,[3,4] states that there is still lack of knowledge of the multiple pathways of pain; also, "Some of these pain mechanisms are very bizarre, and even today our knowledge of the complex functions of the central and autonomic nervous systems is indeed elementary." In discussing Adams' paper, Barrett says, "The sympathetic nervous system is a dominant factor in pain; except for direct nerve trauma, ischemia, or localized hypoxia, it is probable that it is the basis of most pain."

Livingston[4] has defined the mechanism of pain as follows: "Pain is a perception; it is subjective and individual; it varies in different races of people; and individual susceptibility to pain may vary with changes in emotional and physical equilibrium." There is evidence that pain may also vary with changes in the endocrine equilibrium; and when the endocrine balance has been disturbed, marked susceptibility to pain can be evident, which disappears when adequate vitamin-mineral balance is obtained along with restoration of depleted endocrine glands, particularly the anterior pituitary and adrenal cortex.

Livingston states that "Pain is believed to be subserved chiefly by neuron units whose fibers branch into a complicated, subepidermal nerve net that eventually terminates in multiple, undifferentiated endings . . . It is customary to speak of 'fast' pain and 'slow' pain

to designate their difference of speed . . . The fast pain sensations are more vivid, less persistent and more readily localizable. The slow pain is diffuse, difficult to localize exactly, reverberating, and impels its victim to squeeze or rub the affected part."

There is a tendency, Livingston writes, that is rather widespread, to use the term "psychic" pain in a loose manner for cases in which there is no obvious organic origin of the pain. He warns "against the indiscriminate employment of the term 'psychic' pain in classifying cases that lack an obvious organic basis for their complaints, or simply because their signs and symptoms fail to conform to the generally recognized patterns of nerve distribution."

Peripheral nerves[5-7] have been shown to contain, besides the somatic fibers, sympathetic motor (vasomotor, sudomotor, pilomotor) and afferent sympathetic fibers conveying pain impulses.

The character of the pain in the segmental neuralgias,[8] caused by irritation of the extraspinal or paraspinal elements that constitute the segmental distribution, may vary from stabbing, tearing, shooting or cramp-like to a milder aching, sore, drawing, pulling, dragging type of pain. Painful areas which are localized "and are tender to the slightest touch, or brushing of wearing apparel or bedclothes, and are associated with burning, suggest a causalgic type of pain which is sympathetic in origin."

The term "atypical neuralgia" is used to differentiate it from the segmented neuralgia on the one hand and to indicate its sympathetic component on the other. As a history of trauma cannot be elicited in all cases of headache, migraine and occipital neuralgia, this designation would be more appropriate than Livingston's "post-traumatic pain syndrome."

Livingston[4] mentions atypical facial neuralgia to call attention to the fact "that trigger points may develop in the face, neck and scalp, just as they do in the extremities or in the back, and that they seem to be capable of initiating pathologic reflexes as do other trigger points; and the fact that they sometimes yield to simple measures suggests that irritation from peripheral sources may play some part in the development of pain syndromes involving the head areas. One of the most interesting types of trigger points that may give rise to pain is represented by small, palpable masses that are designated by the term 'myositis.' It is well known that a form of headache may develop secondary to the appearance of discrete kernels at the base of the skull and in the upper part of the neck. Sometimes they feel as if they were in the subcutaneous tissue. They are tender to pressure, so that massage may be painful, but this form of treatment may be most effective in dispelling their tenderness." I, too, have found these so-called areas of myositis, which if injected with procaine momentarily elicit a painful response referred to areas similar to but not exactly those of peripheral nerves. In some instances, after a viral infection such as mumps, small discrete, movable, sensitive, subcutaneous nodules are found usually along vessels. Injection of these nodules with procaine results in considerable or complete relief of the atypical neuralgia. However, much more commonly, the trigger point is not represented by a palpable mass, and here a point of deep tenderness in the scalp, occipital muscles, at the ends of the transverse processes of the cervical vertebrae or beneath the superficial layers of the skin may be found as the trigger point although there is no other indication of a local pathologic condition.

Migrainous headaches may come in attacks initiated by fatigue, menstruation, food idiosyncrasy and other exciting causes. The underlying neurologic mechanisms which produce the hemicrania and such other disturbances as hemianopsia, paresthesias, ophthalmoplegia, unilateral pallor or flushing, lacrimation and nasal congestion indicate involvement of the sympathetic nervous system.

Wolff[1] and associates have shown that the cranial and scalp vessels are implicated in the migrainous headache and that it could be abolished by mechanical obliteration of the temporal and occipital arteries. The mechanism of the atypical neuralgias of the head and face is the same as that of migraine, namely, irritation of sympathetic fibers in the tissues as well as in the walls of blood vessels. In migraine, Wolff believes that the therapeutic effect of ergotamine tartrate depends upon its ability to constrict the relaxed scalp and facial vessels. However, adjacent procaine infiltration may cause further dilation of these vessels, yet the headache is relieved at once. Furthermore, accurate localization and injection with 2 per cent procaine of trigger points may not only

stop the headache immediately, but also this relief often lasts for months or years.

In occipital neuralgia a history of soreness or stiffness in the neck with limitation of motion may precede or be associated with the headaches which usually begin in the occipital area, radiating to the frontal or supraorbital region. The headaches are frequent, almost daily, and are usually prolonged and recurrent for weeks or even years. They are steady and vary from a mild ache to a severe, throbbing, bursting pain, worse on stooping or straining at stool. At times the frontal headache is so predominant that painful symptoms referable to the occipital region or neck are submerged, but sensitive areas are readily found across the occiput or along the spines or transverse processes of the upper cervical vertebrae.

When the pain from sensitized spots of the head has been sufficiently long in intensity and duration, painful contraction of the skeletal muscles of the head, neck, shoulders and even the erector spinalis group in the lumbar region may develop and produce further involvement.

Twenty-five years ago I noted that the toothache pain, often of a burning character, is still present during the extraction of an impacted lower wisdom tooth under repeated block anesthesia of the third branch of the fifth nerve. This pain comes only when blood vessels are encountered, is undoubtedly of sympathetic origin and reaches the sensorium other than by way of the fifth nerve.

One patient was referred for trigeminal neuralgia who complained of repeated stabs of pain in the upper left incisor tooth, coming rapidly like that of an air drill, and who was sensitive to touch along the upper part of his lip. We observed that the stabs of pain were synchronous with his heart beat and that firm pressure on the left facial vessels as they passed over the mandible momentarily stopped the pain. Excision of these vessels with the accompanying loose tissue showed on histologic examination many non-myelinated fibers not only in the walls and close to these vessels, but also 1 to 2 cm. on either side of these vessels. The pain was relieved and this treatment for atypical facial neuralgia or buccal neuralgia[9] was reported.

About this same time, in 1930, a patient was seen four and a half years after he had been thrown from a truck (industrial accident), causing a short period of unconsciousness followed by persistent headache and light-headedness or "dizziness" which rendered him unable to work his ranch. He was seen by many neurologists and neurosurgeons. The neurologic findings had never shown any abnormality and two air encephalograms were normal, so that his condition was diagnosed finally as psychoneurotic in origin. He volunteered that if he pressed hard on certain spots in the occipital region, the headache could be relieved temporarily. These spots, six in number, were located with the rounded but rather pointed end of a fountain pen and 2 per cent procaine was injected down to the periosteum in each of these trigger points. His headache was relieved completely and he then could stoop over without any "dizziness" and without causing a headache. He remained cured and his compensation was stopped.

Penfield[10,11] has written of the treatment of localized, post-traumatic headache and dizziness, first by spinal, subarachnoid air insufflation, and later by subdural air insufflation, the air being directed by positioning the head to the area of localized headache. This often gives spectacular relief.[12] However, this treatment, done for its diagnostic as well as its possible therapeutic effect, is of no help in those patients who have rather generalized headache following trauma and in whom repeated neurologic examinations remain negative. In 1944 Jones and Brown[13] reported some relief of these symptoms by procaine injections in the upper cervical region. In patients of this type trigger points can be found by careful search in areas over the occiput and cervical vertebrae; also, in the frontal, orbital and maxillary areas penetrating fibers are known to exist which, when injected with procaine, give immediate relief.

In Gay and Abbott's[14] recent interesting report on common whiplash injuries to the neck which produce sprain of the neck resulting in headache and cervical radiculitis, there is mechanical trauma with likely hemorrhage and edema in the region of the damaged ligaments that subsequently undergo fibrosis and cicatricial changes that may be a chronic source of irritation. The authors found 81 per cent of fifty patients improved and 19 per cent well under conservative treatment of rest, intermittent head traction and hydrotherapy in which recovery was slow and complicated by a psychoneurotic reaction in most cases.

Thirty per cent of their patients had injury to the lower back due to mechanical trauma of the supporting ligaments of the lumbar spine.

After trauma other than sprain from a whiplash injury, such as slipping and trying to prevent a fall, the occipital and neck muscles

FIG. 1. The cross marks indicate the location of the usual trigger points. (Modified from Sobotta's Atlas of Human Anatomy. Philadelphia. W. B. Saunders Co.)

may be strained. The sympathetic nervous system can become sensitized after certain infections, notably virus diseases, influenza, recurrent attacks of malaria, rheumatic fever, dengue or acute infections of the upper respiratory tract.

Subsequent to trauma or contusion, fine unmyelinated afferent nerve fibers have been found injured in scar tissue. Graham[15] believes these injured fibers have a lower threshold and therefore ordinarily non-painful stimuli cause the patient to experience pain. Because of the fact that many of these patients have had their headache or neuralgia for months or years, a self-sustaining cycle has been established with a lowering of the threshold for pain and a continuous mild alarm reaction with depletion of the adrenal cortex and/or the anterior pituitary.

Very frequently the patient with headache will find the scalp sensitive to touch or brushing and can designate points on or near vessels that are very tender and which, subjected to firm pressure, will temporarily relieve the symptoms. During a headache, along with an aching in the neck, there may be limitation of motion of the head and neck. Slight trauma or a mild whiplash injury, perhaps forgotten, may have produced injury in the nature of a strain to the cervical paravertebral ligaments, to the fascial attachments of the short rotator capitis muscles, to the vertebral processes or to the trapezius and rhomboid attachments to the vertebrae or scapula. Tenderness between the cervical spines or near their transverse processes is frequently found. Trigger points in the posterior neck must therefore be searched for and injected with the usual trigger points across the occiput, in the temples and supraorbitally if complete relief of headache or neuralgia is to be secured. (Figs. 1 to 3.)

Another source of irritant sympathetic nerve endings is the loose areolar tissue and potential bursa in the interspinous ligament (Fig. 4) located between the vertebral spinous processes. The point of the needle for injection must penetrate only as far as the transverse arch or to the ligamentum flavum since a deeper injection of the 2 per cent procaine will enter the spinal canal where it may do damage.

Trauma to the head and neck, often in childhood and long forgotten, may tear loose the ligamentum nuchae from the cervical spinous processes. When the head is bent forward, this shredded ligament forms a bow-string from the occiput to the last cervical or first thoracic spine. Trigger points are to be found in this ligament or deeper between the spinous processes or at the ends of the ligament. (Fig. 2.)

Raney et al.[16] believe that occipital neuralgia may be caused by high cervical, herniated intervertebral disc, and report good results after operation. However, during surgical exposure for intervertebral disc many or all of the trigger points are destroyed and the headache is therefore relieved.

Josey[17] states, "The pathologic change in the cervical region as a cause of headache has been the subject of medical writings for many years." His paper emphasizes the roentgenographic demonstration of a loss of the normal lordotic curvature of the cervical portion of the spine in his patients with headache. Treat-

ment by immobilization of the head and head traction afforded temporary or semi-permanent relief in some of his twenty patients. Because other writers had reported only temporary relief from procaine injections into localized areas in the suboccipital region, his painstaking injection of the sensitized areas. The trigger points are located by making pressure first with the rounded end of a ball-point pen and then its tip, progressing tangentially toward maximum sensitivity, and these are rechecked several times making pressure

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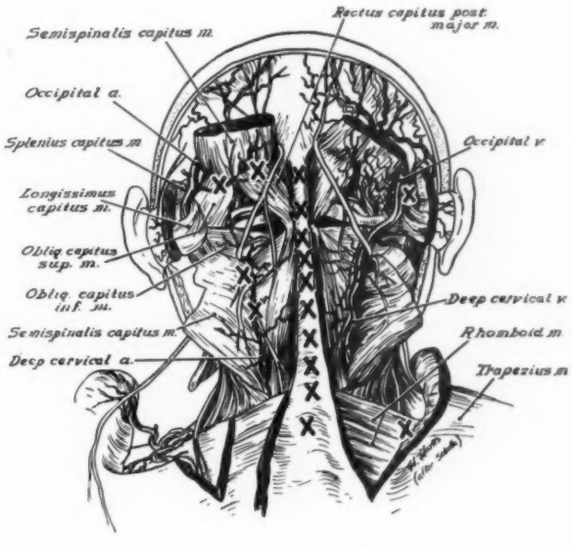


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FIG. 2. The cross marks indicate the location of the usual trigger points. (Modified from Sobotta's Atlas of Human Anatomy. Philadelphia. W. B. Saunders Co.)

FIG. 3. The cross marks indicate the usual trigger points. The vertical cross marks are between the cervical spinous processes where the torn ligamentum nuchae makes a "bow string." (Modified from Sobotta's Atlas of Human Anatomy. Philadelphia. W. B. Saunders Co.)

series included only one such case with no permanent relief.

A number of my patients had previously had head traction elsewhere, with little or no relief. Perhaps Martin and Corbin's[18] heavy head traction for only one to three minutes twice daily in patients with cervical disc syndrome might have been more effectual. However, when all of the trigger points of the head and neck have been injected with procaine, not only do the patients have complete freedom from headache and can again move the head and neck in all directions freely, but also the normal lordotic curvature of the cervical spine reappears. Reinjection of areas in the posterior neck that may not have been localized with sufficient accuracy is at times necessary to secure permanent relief.

In describing the method of injecting trigger spots with 2 per cent procaine, I wish to emphasize the most accurate identification and in the same direction. Finally they are marked so that when the fine No. 25 needle with a very short bevel is introduced, exactly the same direction is followed as with the pen. The deposition of 2 per cent procaine is begun just beneath the skin and made gradually deeper until all trigger points have been reached. Usually from 2 to 5 cc. are injected in each area and not more than 40 or 50 cc. are injected at a visit.

Hematologic studies have been found to be normal in those patients who bruise easily; and since a hematoma at the site of injection vitiates the success of the treatment, 10 mg. of vitamin K are injected subcutaneously before treatment, and ½ gr. of phenobarbital is given by mouth at least twenty minutes before the injection is started.

No patient receives an injection of procaine, no matter how small in amount, without first receiving a barbiturate which reduces the

toxicity of procaine about five times. Patients who are known to be sensitive to procaine receive ½ gr. of phenobarbital orally three, two, one, and one-half hour before treatment. An ampul containing 2 gr. of sodium phenobarbital is always available, half to be given

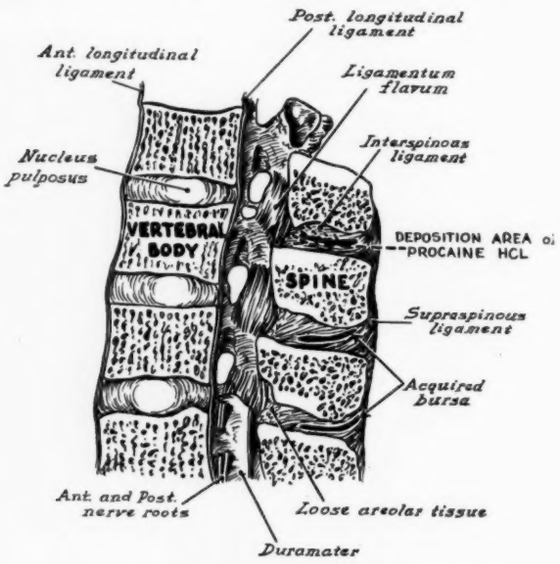


FIG. 4. Showing the location of the ligamentum flavum, the interspinous ligament with its bursa. The needles for procaine injection penetrate between the spinous processes into the interspinous ligament and bursa down to the transverse arch or the ligamentum flavum. (Modified from J. C. B. Grant's Atlas of Anatomy. Baltimore, 1947. Williams & Wilkins Co.)

intramuscularly if a patient should have a reaction to the 2 per cent procaine. One-half cubic centimeter of adrenal cortical extract subcutaneously is also given.

The long-continued headache or pain has furnished the alarm reaction as described by Selye,[19] with depletion of the patient's adrenal cortex in particular and frequently also the anterior pituitary, as evidenced by their excessive perspiration or tendency to cry easily.

In restoring impaired endocrine glands such as the anterior pituitary and adrenal cortex, a high protein, high vitamin C diet is essential. Myers[20] pointed out several years ago that the desiccated glandular preparations function best in the presence of multivitamins and minerals which are given along with digestive enzymes, pancreatin and bile salts to aid their absorption. A suprarenal tablet, 3 gr., is taken daily with the vitamins before a meal. For exhaustion, one or more of these suprarenal tablets are given during the day; for perspiration or weeping tendency, one or more anterior pituitary tablets, 5 gr., are sucked until relief is obtained. Potassium chloride, 15 gr., is given daily to protect the cellular potassium from the effects of these hormones.

In a certain few patients with depleted anterior pituitary gland but active adrenal cortex, either the injection of anterior pituitary extract or sucking several 5 gr. desiccated anterior pituitary tablets will stop the headache. Since June, 1954, we have found that these headaches as well as the tendency to cry or to have profuse perspiration could be relieved by the action of the Rauwolfia root or its alkaloid, reserpine.[21] For the first time we had a substance that would at least partially suppress the sympathetic predominance at the hypothalmic level. Usually within two weeks of taking a Rauwolfia preparation the effect on headache, crying or sweating is noticeable and there is no need for further anterior pituitary substances except occasionally. Calcium is given in some form, by mouth or injection, to reduce the excitability of the neuromuscular apparatus. It is an interesting and important observation that patients free of pain and physically well will discontinue the daily vitamin-mineral-suprarenal cortex therapy and within three to six weeks have their pains or headache return. On resumption of medication the headaches or pains disappear usually within a month.

Many of the patients have learned that alcohol will cause a return of their headache or pains in the course of two to six or eight hours. Two patients who were injected unknowingly after having a high alcoholic intake were not relieved; yet later when the alcohol was out of their system, the injection treatment was successful. Several patients who were not truthful about taking alcohol between visits had to be reinjected at intervals of three or four weeks until they understood the importance of abstinence. From these observations it is believed important to instruct all patients about the probable effects of taking alcohol in any form. Some patients after several months of adequate vitamin maintenance and endocrine balance seem capable of partaking without recurrence of their pains, yet others have found abstinence to be the best policy.

A brief summary of the history and treatment of two of the seventy-eight patients follows.

## CASE REPORTS

CASE 1. E. C., a forty-three year old woman, was thrown from a horse in 1943. In 1945 headaches started with a stiff neck and continued daily until November, 1949, when a series of three treatments was given of forty-three injections of trigger points about the head and neck muscles and transverse processes of the upper three cervical vertebrae. She was started on daily multivitamin therapy with added vitamins B and C and bile salts at this time. One year later she wrote that instead of having headaches 80 per cent of the time they were present only 10 per cent, and their intensity was reduced to only 15 per cent. She believed she was practically cured as far as the headaches were concerned, but did complain of aches in other parts of her body. In February, 1951, she returned for injections between the spinous processes of the lower cervical and all except the last two thoracic vertebrae, and several points on the anterior ribs where the origins of the pectoral muscles had been strained in her fall. At this time suprarenal cortex tablets, 3 gr., were given twice weekly. Her monthly reports have been interesting as she became physically fit and her pains and aches disappeared. At the end of April, 1951, she wrote, "I never dreamed that I should ever know what it was to feel well day after day." In June she wrote that her friends said she looked "better than I did ten years ago." On August 29th her physician injected trigger points in her sacroiliac region and reported that he had never seen her in better condition. She was last heard from at Christmas, 1953.

CASE II. G. V., a twenty-three year old man, was first seen on June 13, 1946. As an Army aviator of two years' training he had been forced to crash land in April, 1945. At this time he sustained numerous scalp lacerations and was unconscious for several days. Subsequent constant headaches led to numerous electroencephalograms, two pneumoencephalograms and finally a disability discharge one year after the accident. Trigger points across the occiput, in the many healed scalp scars, and in the temporal and supraorbital regions were injected with 2 per cent procaine, with surprising relief to the patient. Dense subcutaneous and fascial scar tissue was encountered with the needle, especially in the occipital region on both sides. The patient was relieved until October, 1946. Reinjections were given and new trigger areas were injected in December, 1946, and January, February, April, July and October, 1947, after he had started work in an office and had found other trigger spots in the lumbar and sacroiliac regions. A cold in May, 1948, started the headaches again but complete relief was given by injections between the spinous processes of the cervical, upper thoracic and lower lumbar regions as well as across the occiput. The patient was well and entered college. Influenza in January, 1949, caused the headaches to return; these were relieved by injection of eight trigger points in the occipital region. At this last treatment in October, 1949, when along with the occipital areas the transverse processes of C2 and C3 bilaterally were injected, he was placed on multivitamin therapy with added vitamins B and C and bile salts. For three weeks in February, 1950, when he did not replenish his supply of vitamins, the headaches returned but improved after he again took vitamins and bile salts for two weeks. Within a month he was well and free of headaches. He is now an interne and has remained well, as reported in December, 1953.

## COMMENTS

As no record or classification of these patients treated in our clinic outpatient department has been kept, I can report only on patients seen privately during the past twenty years and can give the follow-up reports on seventy-eight such patients. (Seventy-one cases were not included in this report, having been lost to follow-up.)

Of the seventy-eight patients, a definite history of headache developing after trauma or whiplash injury was noted in thirty. In seventeen patients there was evidence of previous trauma by the tearing loose of the ligamentum nuchae from the cervical spines, producing the "bowstring" or taut cord extending from occiput to about the seventh cervical spine.

Thirty patients seen before 1951 had their trigger points injected with 2 per cent procaine. Sixteen or 53 per cent remained free of their headaches, eleven or 37 per cent received no relief from the injections, and three who were well for a short time after the injections have not answered our inquiries.

Forty-six patients received the 2 per cent procaine injections and were given daily vitamins, adrenal cortex and/or anterior pituitary tablets. Thirty-three of these patients or 72 per cent have remained free of their headache from one to four years. Four or 8.7 per cent received no relief and three were well for a short time after injection but have not replied to subsequent inquiries. Six have had 80 per cent relief of their headaches, having only an occasional mild pain.

Many of the patients who were well after injection of trigger points had suffered only a short time from headaches. Others who were injected without relief might have been helped if vitamins and hormones had been given.

After 1951, when we learned of the advantages of vitamin and hormonal therapy for patients who were depleted, the percentage rose to 85 of those relieved of headaches (including six patients with 80 per cent relief).


## SUMMARY

Relief of atypical neuralgias of the head and face, occipital neuralgia and migrainous headache may be secured by painstaking and accurate injection of 2 per cent procaine into the sensitized trigger points, repeating the injections if necessary until all trigger spots have been abolished.

The sensitized trigger points are caused by trauma, toxins or compression of the small unmyelinated sympathetic fibers in and accompanying blood vessels, and in the subcutaneous tissues, muscles, fascia, ligaments and attachments of muscles to bone.

The usual location of these trigger points for the various types of neuralgias of the head and neck has been described and illustrated.

Sensitized areas from strains or sprains, such as occur in whiplash injuries, involve the deeper posterior rotator neck muscles, and trigger points are found in the interspinous ligament and its bursae, between the spines of the cervical vertebrae and the strained attachments of muscles to the transverse processes of these vertebrae.

From these locations may originate the referred pain to the occipital and frontal parts of the head, face, shoulders and even down the back.

To prevent recurrence of the neuralgia after injections of the trigger points, especially in patients depleted from long-continued pain causing repeated mild alarm reactions, vitamins and adrenal cortex and/or anterior pituitary preparations in particular are given.

Recently the use of the Rauwolfia root or its alkaloid, reserpine, for suppression of the sympathetic predominance at the hypothalamic level has served better than anterior pituitary substances in relieving headache, crying or the profuse perspiration that some patients experience.


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# Surgery of the Adrenals

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IN 1945 a fifty year old man, incapacitated by severe drenching sweats, was examined and found to have moderate persistent hypertension, mild obesity and warm moist skin. Laboratory studies disclosed a trace of sugar in the urine, a basal metabolic rate of plus 45, and a normal chest film and intravenous pyelograms. The association of hypertension, profuse sweating, mild glycosuria and hypermetabolism led to a clinical diagnosis of pheochromocytoma. Bilateral simultaneous adrenal exploration was performed. A large left adrenal pheochrome tumor was found and removed without undue trauma or difficulty. Immediately thereafter the patient became desperately ill with uncontrollable hypotension and severe hyperpyrexia. He died from adrenal crisis within twenty-four hours.

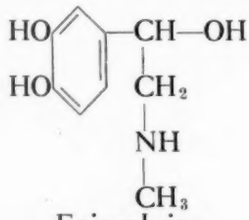
Such was the history of adrenal surgery in many cases in 1945. The past ten years have not only led to improvements in the technical aspects of adrenal surgery but also have witnessed the development of methods for maintenance of life in the total absence of the adrenal glands and the perfection of diagnostic procedures for the assessment and localization of adrenal disorders. Huggins and Dao[1] have recently reported 100 bilateral total adrenalectomies in patients with metastatic breast carcinoma with an operative mortality of only 5 per cent, but with no deaths from postoperative adrenal crisis. Adrenal surgery has reached the stage of technical safety. Judgment as to its proper indications requires continued clarification, and frontiers in the application of adrenal surgery to the alteration of bodily functions remain to be explored.

The present paper is a brief summary of the existing state and basic concepts in adrenal surgery.

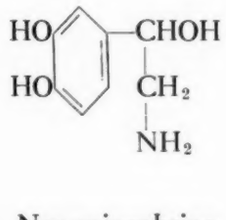
## BASIC CHEMISTRY AND PHYSIOLOGY

The anatomic association of the adrenal cortex and medulla seems quite fortuitous, for embryologically, functionally and physiologically they are quite different. The adrenal medulla originates from ectodermal pheochromoblasts along the developing sympathetic ganglionated chain and consists of masses of polyhedral chromaffin cells. It produces two hormones, epinephrine and nor-epinephrine, and its activity is controlled largely by the sympathetic nervous system. It is not under pituitary control, and its total absence is compatible with life. The adrenal cortex, on the other hand, arises from mesothelium of the genital ridge, consists of three distinct histologic layers which produce a wide variety of hormones related to water, salt, carbohydrate, fat, protein and androgenic metabolism, is not controlled by the sympathetic nervous system, is under pituitary control, and is essential for maintenance of life. The assignment of distinct physiologic functions to each cortical zone is not exact, but the glomerulosa seems to be the predominant source of the electrolyte hormones and is less dependent on pituitary control.

*The Adrenal Medulla.* The normal adrenal medulla and also pheochrome tumors of the adrenal medulla produce two hormones: epinephrine and nor-epinephrine. These hormones differ chemically only by the absence of a methyl group on nor-epinephrine.



Epinephrine



Nor-epinephrine

Physiologically, however, the action of these two hormones is quite different. Epinephrine seems to be the hormone mediating the general body reactions to stress, influences the pituitary output of adrenocorticotropin, and redistributes blood flow generally, diverting flow away from the skin and intestinal viscera and into the muscles, brain and heart. With epi-

nephrine the total peripheral vascular resistance declines due to this redistribution of flow, the cardiac output is increased and the blood pressure rises. Nor-epinephrine, interestingly enough, mimics more closely the effects of sympathetic efferent stimulation, and in fact,

TABLE 1

| Cardiovascular Function | Epinephrine | Nor-epinephrine |
|---|---|---|
| Pulse rate | Increased | Decreased |
| Cardiac output | Increased considerably | Little change |
| Systolic blood pressure | Increased | Increased |
| Diastolic pressure | Slight change | Increased |
| Total peripheral resistance | Decreased | Increased |
| Oxygen consumption | Increased | No change |
| Blood sugar | Increased | No change |
| Corticotropin output | Increased | No change |

is the chemical mediator for synaptic transmission at the sympathetic nerve end-plate. It produces generalized vascular constriction regardless of the vascular bed on which it acts, raises the total peripheral vascular resistance, elevates the blood pressure, has a variable effect on cardiac output and coronary blood flow, and does not induce an increased corticotropin output from the pituitary. Goldenberg has studied in detail the actions of these two hormones in humans, and Table 1 is modified from his paper.[2] Nor-epinephrine seems to permit a more localized and regional control of vascular tone and blood flow, and may be more significant in the control of peripheral vascular resistance and blood pressure.

*The Adrenal Cortex.* The basic chemical structure of the adrenocortical steroids is the sterol nucleus. This sterol nucleus is the basic component of many biologically active substances ranging from cholesterol to bile salts to sex hormones. Chemical investigations have disclosed at least twenty-eight adrenal cortical steroids, but the biologic activity of only a few of these has been carefully investigated. Biologic activity is largely controlled by radicals attached to the 11 and 17 bonds. The desoxycorticosterones with no attached oxygen or hydroxyl radicals at the 11 carbon bond influence electrolyte metabolism predominantly, and recently aldosterone has been identified with almost pure sodium-retaining effects.[3] (Desoxycorticosterone and 17-hydroxydesoxycorticosterone are examples of this type.) An adrenal steroid with an oxy- or hydroxyl group at the 11 carbon position has a marked effect on carbohydrate metabolism, causing formation of carbohydrate from protein and glycogen deposition in the liver. These 11-oxy or 11-hydroxy steroids have some effect on electrolyte metabolism as well, and less marked effects on fat and protein metabolism. (Corticosterone, 17-hydroxycorticosterone, cortisone and 11-dehydrocorticosterone are examples of this type.) The chemical structure of these adrenal steroids and their synonyms are illustrated in Figure 1 for additional clarification of terminology and composition.

Studies in the genesis and biosynthesis of adrenocortical hormones[4] employing the methods of adrenal perfusion with isotopic cholesterol suggest strongly that the principal hormones elaborated by the cortex are compounds F and B, the two 11-hydroxycorticosterones. Compounds E and A, the corresponding 11-oxy compounds are probably reversible oxidation products of the former two compounds with similar but less striking physiologic effects. The 17-ketosteroids seem to be intermediate or breakdown products of the principal corticosteroids. The 11-desoxycorticosterones also seem to have their origin from cholesterol. The metabolic pathway compatible with available evidence suggests that cholesterol is degraded first to pregnenolone by oxidation, the latter is further oxidized to progesterone, and subsequent hydroxylation at the 21 position yields 11-desoxycorticosterone; at the 11, 21 position corticosterone; and at the 11, 17, 21 position hydrocortisone. The adrenal cortex does not contain significant reserve stocks of its own hormones, but is capable of rapid synthesis of these hormones from cholesterol.

Hypophysectomy results in atrophy of the adrenal cortex but life is maintained through a steady minimal secretion of adrenocortical hormones. The pituitary, nevertheless, exerts an important regulation in secretion of adrenocortical hormones (ACE) through its hormone, adrenocorticotropin (ACTH). The two prime controlling factors in the elaboration of ACTH are: (1) the level of circulating adrenocortical hormones in the blood and tissues, and (2) the nervous system and epinephrine. Stress in-

creases the utilization of ACE by the tissues, the reciprocal inhibition of ACE on ACTH production is diminished, and the pituitary elaborates more ACTH, thereby augmenting the output of adrenocortical hormones during stress. This is a slow mechanism mediated over a period of hours or days.

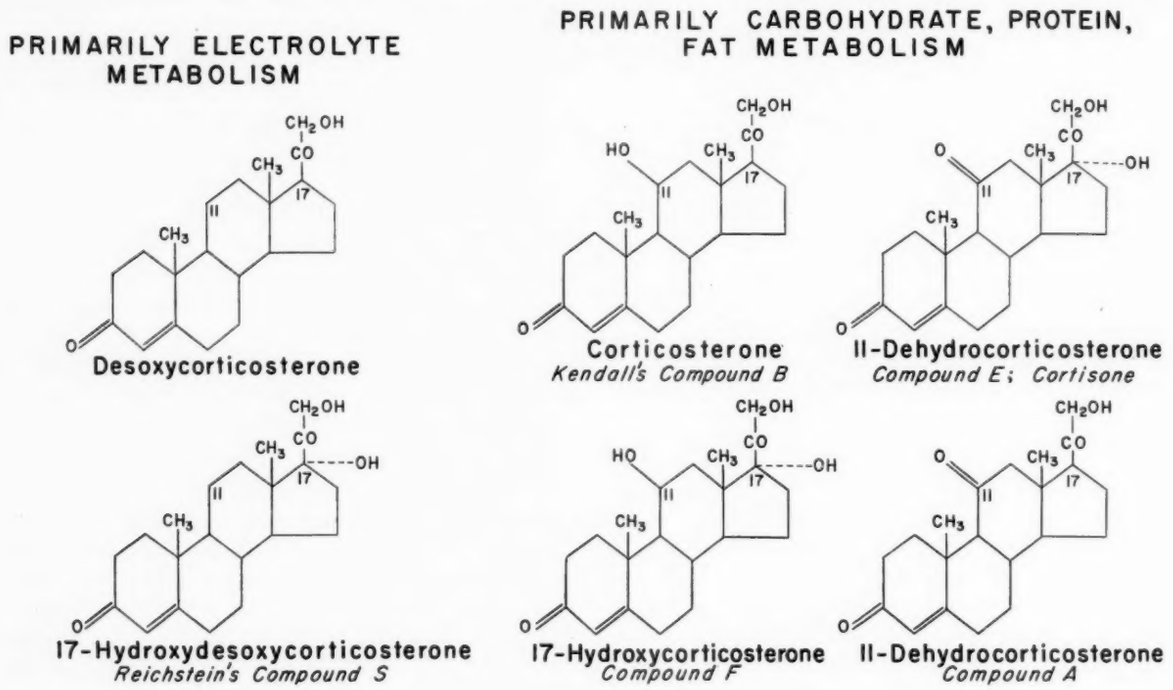



FIG. 1.

Another more immediate and rapid mechanism of control of ACTH production is through the release of epinephrine by increased activity of the sympathetic nervous system. Similarly, somatic nervous system stimulation and hypothalamic stimulation, either directly or indirectly, can alter the production of ACTH. Epinephrine cannot only increase the peripheral utilization of ACE but can also act directly on the hypothalamus and pituitary to increase the production of ACTH. Epinephrine aids very decidedly, therefore, in the response to stress and serves as a more rapid mechanism of ACTH control than the slower but more prolonged ACE mechanism. Figure 2 illustrates the metabolic and autonomic phases of ACTH control.

## TUMORS OF THE ADRENALS

Much of our knowledge about the adrenals stems from a study of clinical disorders of the adrenal glands. From the surgical viewpoint tumors and hyperfunction of both the cortex and medulla have required treatment rather than evidences of hypofunction which, if cortical in site, results in Addison's disease. The common tumors of the adrenals may be classified as follows: (1) Tumors of the cortex including (*a*) experimental cortical tumors, (*b*) Cushing's syndrome—corticoid effects, (*c*) androgenic tumors and (*d*) estrogenic tumors. (2) Tumors of the medulla including (*a*) non-endocrine—neuroblastomas, sympathetic ganglion cell tumors which may originate from immature cells (sympathoblastoma) or mature cells (ganglioneuroma) and (*b*) endocrine—the pheochromocytomas.

*Tumors of the Cortex. Experimental cortical tumors:* The concept that tumors of the host might be related to the endocrine environment of the host, particularly tumors of the adrenals, was elucidated by Woolley and Little.[5] Gonadectomy in susceptible strains of mice soon after birth resulted in hyperplasia of the adrenal cortex, followed by metastasizing and transplantable tumors in close to 100 per cent of the animals. The pituitary is essential to the production of these tumors, and they may be prevented (apparently from pituitary inhibition) by administration of estrogen to castrated mice. These concepts have

been extended clinically by Huggins and Dao[1] in the management of carcinoma of the breast, and will be discussed later.

*Cushing's syndrome:* Cushing's syndrome is produced most commonly by adrenal cortical tumors elaborating an excessive amount of corticoids, but can result from cortical hyperplasia. A pituitary basophilic adenoma is not essential to the condition, but the pituitary basophils lose their granules and develop hyaline changes (Crooke cells). Cushing's syndrome occurs most frequently in women of young adult years. Truncal obesity, hypertension, hirsutism, "moon face," osteoporosis and purplish striae of the skin are the most prominent clinical features. Mild diabetes, menstrual abnormalities, weakness and mental aberrations are less striking. The association of hypertension with Cushing's syndrome and its relief by removal of the adrenal cortical tumor or hyperplasia is worthy of special comment, and has led to more careful study of the relationships of the adrenals to essential hypertension. Many excellent discussions of the significance of each symptom of Cushing's syndrome are available, and the symptoms and signs frequently encountered are listed in Table II.

It is apparent from Table II that the prime effects result from an excessive production of corticoids (Compounds B, F, A and E), but that some symptoms result from an increased secretion of the salt-retaining hormones (DOCA and aldosterone) and the androgenic and estrogenic substances.

The laboratory findings are similar to those encountered after prolonged corticotropin administration. The most frequent and consistent laboratory finding is a diminished carbohydrate tolerance with hyperglycemia and a diabetic type of glucose tolerance curve. Overt diabetes is uncommon but glycosuria, which is rather

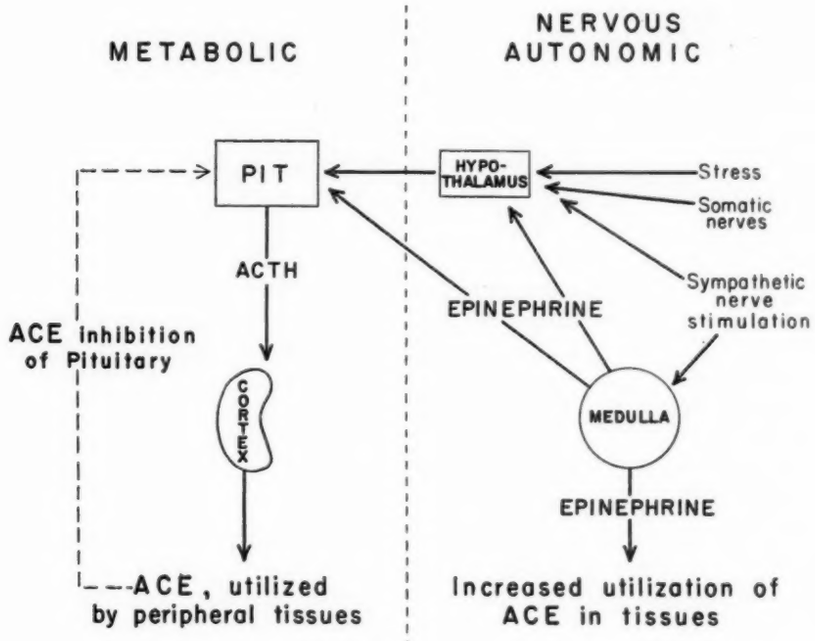



FIG. 2.

TABLE II

| Symptom | Approximate Occurrence Rate (%) |
|---|---|
| Obesity, altered body habits, facial and abdominal obesity | 95 |
| Hypertension | 85 |
| Menstrual disturbances, virilism, impotence | 70 |
| Hirsutism | 70 |
| Purplish striae and ecchymosis | 60 |
| Weakness, backache, fatigue, atrophy | 50 |
| Osteoporosis, diabetes, hypochloremic, alkalosis | 30 |
| Mental abnormalities, mild | 25 |

resistant to insulin, is frequent. X-ray evidence of demineralization of bone is very common, particularly in the spine and skull. The twenty-four-hour urinary excretion of corticoids is generally increased. The urinary excretion of 17-ketosteroids may be normal, but tends to be high in the cases of adrenal hyperplasia and adrenal cortical carcinoma rather than in the benign adenoma group. The administration of cortisone, by suppressing ACTH production, will drop the 17-ketosteroid excretion in cases of hyperplasia but not in those of autonomous adrenal adenomas.

In the blood serum there is a tendency to hypochloremic alkalosis with an elevation of serum sodium and a lowering of serum potassium. Azoturia results from the negative nitrogen balance, and osteoporosis results from a mobilization of bone calcium with associated hypercalcemia. Eosinopenia and lymphocytopenia occur frequently.

The diagnosis of Cushing's syndrome depends primarily upon the clinical picture, the laboratory findings and the x-rays, but in occasional cases certain additional adjuncts are necessary. Since these diagnostic adjuncts apply equally well to the lesions of medullary origin they will be discussed separately. Presacral air injection followed by x-ray visualization of the adrenal areas has become the most accurate method of tumor localization prior to surgical exploration.

Present treatment of Cushing's syndrome is directed toward the adrenals. No longer is irradiation therapy to the pituitary employed. Regardless of smouldering arguments about the primary cause of the disease being in the pituitary or even the thymus, the clinical features result from hyperfunction of the adrenal cortex. If an adrenal tumor is present it should be resected. Furthermore, Priestley et al.[6] have clearly shown that in the absence of a functioning tumor extensive resection of the adrenals produces complete remission of the disease in most cases. Equally significant is the observation that hyperfunction of the adrenal cortices can exist in the absence of gross adrenal enlargement. The accepted concept of radical subtotal adrenal resection is to remove one gland completely and 90 per cent of the remaining gland.

In former days it was difficult to justify radical subtotal adrenal resection for Cushing's syndrome, for the risk of surgery alone was great in these patients. Nowadays, however, bilateral complete adrenalectomy can be performed with a mortality rate of 5 per cent or less, due to the availability and understanding of the use of adrenal hormones pre- and postoperatively. The prognosis in untreated Cushing's syndrome is grave, with a mortality of 50 per cent by the end of five years from infections, cardiovascular accidents, uremia and so on. With no other satisfactory methods of treatment and with the results thus far demonstrated with extensive subtotal adrenalectomy, adrenal surgery is well justified in Cushing's disease even if a tumor does not exist. Pre- and postoperative therapy will be discussed later.

*Adrenogenital syndrome:* Adrenal cortical hyperplasia and adrenal cortical tumors may produce virilization, increased growth and muscularity, and accelerated epiphyseal ossification without the associated signs of corticoid hypersecretion of Cushing's syndrome. This is commonly called the adrenogenital syndrome.

The clinical picture depends upon the time in development at which excess production of androgens occurs. Adrenal hyperplasia prior to intrauterine differentiation of the sex organs results in "macrogenitosomia precox" in the male or "pseudohermaphroditism" in the female; adrenal hyperplasia or tumor after differentiation of the sex organs results in virilization, feminization, or precocious sexual development. The female pseudohermaphrodites show a urogenital sinus with the vagina opening into the urethra at approximately the level of the perineal membrane, marked enlargement of the clitoris with the seeming appearance of a hypospadias and some union of the labioscrotal folds into an empty unformed scrotum. In the older age groups masculinization, feminization, clitorine or penile enlargement, pubic hair growth and precocious pubertal development occur. During their infant years either males or females may suffer from acute episodes of weakness and vomiting resembling Addisonian crises, and this is perhaps due to a deficiency of electrolyte-regulating hormones for the serum sodium is low and the potassium high during these periods. Death may occur in these crises.

The tumors may be adenomas or carcinomas, and in the absence of metastases exact diagnosis depends on histologic appearance. The differentiation of adrenal tumor from adrenal hyperplasia is important but difficult. The late

onset favors tumor; abnormalities of fetal development favor congenital hyperplasia. In both, the 17-ketosteroid excretion will be high, but much higher figures will be reached in the tumor cases and it is not possible to reduce the ketosteroid output by the administration of cortisone.

At the present time in cases in which no tumor of the adrenal gland is present, treatment with cortisone is advocated since it rapidly drops the output of ketosteroids to normal, reverses the abnormal sodium and potassium levels in the blood, and reverses the virilizing trend in older children and adolescents. Whether cortisone will prevent the premature epiphyseal ossification is not known.

If a tumor is present, as indicated by the failure of cortisone to drop significantly the ketosteroid output, or if additional studies establish the diagnosis of a tumor rather than hyperplasia, surgery is indicated. The surgical technic will be discussed later.

*Tumors of the Medulla. Neuroblastomas (non-endocrine tumors):* Neuroblastomas constitute a common abdominal tumor of childhood and have been described under various names depending upon the maturity of the tumor cell (sympathogonioma, sympathoblastoma and ganglioneuroma). The sympathoblastoma is highly malignant, arises from immature cells and metastasizes early. The ganglioneuroma is a benign, slowly growing, encapsulated tumor arising from adult ganglion cells of the sympathetic nervous tissue.

Neuroblastomas are encountered in the first few years of life most commonly, but can occur in childhood or later life. An abdominal swelling is the usual presenting complaint. Pain, weight loss, pallor, fatigability and loss of appetite follow. Physical examination reveals a palpable abdominal mass. X-rays of the abdomen show the tumor mass.

Neuroblastomas cannot be distinguished with certainty preoperatively from Wilm's embryoma of the kidney or a retroperitoneal tumor. Surgical removal is indicated since some of the tumors can be completely removed and others diminished significantly in size so that subsequent radiation therapy is more feasible. The abdominal approach to these tumors is preferable since it affords a wider exposure with more complete removal.

*Pheochromocytomas (endocrine-producing tumors of medulla):* These are chromaffin cell tumors that produce both epinephrine and nor-epinephrine. They are physiologically malignant but usually pathologically benign. About 10 per cent of these chromaffin tumors are extra-adrenal in location, being located any place along the sympathetic nerve chain, but usually in the retroperitoneal areas. They are not uncommonly bilateral and rarely metastasize.

The usual symptoms in pheochrome tumors are sudden palpitation, profuse unexplained sweating, blanched cold extremities, severe pounding headache, nervousness, dizziness and precordial distress. Paroxysmal hypertension is classically present during these paroxysmal attacks. Sustained hypertension develops in about one-third of the recorded cases. Atypical hyperthyroidism with an increased basal metabolic rate is occasionally present, and mild glycosuria is not uncommon. A symptom-free individual with sudden collapse, heart failure, or severe hypertension with intense angina should be suspected of having a pheochromocytoma. Pheochrome tumors have been classified into the following types by Richards and Hatch:[7] (1) the adrenal-sympathetic syndrome —paroxysmal hypertension; (2) sustained hypertension, particularly in a young individual or in an adult after pregnancy. This is so frequent that no patient with hypertension may be treated by sympathectomy without bilateral adrenal exploration; (3) atypical hyperthyroidism with increased basal metabolic rate but without thyroid enlargement or other signs of hyperthyroidism; (4) hypertension, mild hyperthyroidism and mild diabetes; (5) a symptom-free individual with sudden collapse or even death following minor trauma or surgery.

The diagnosis of a pheochrome tumor can be suspected clinically, but its verification may require bilateral adrenal exploration. Certain diagnostic adjuncts are most helpful, however, prior to surgery and since these apply also to adrenal cortical tumors they will be discussed under a separate heading. Removal of pheochrome tumors is attended by two hazards: (1) crises during the operative procedure from severe uncontrollable hypertension and (2) collapse during the early postoperative period from adrenal cortical insufficiency. The management of the hypertensive hazard during the operative procedure prior to ablation of the tumor can now be aided by the adrenolytic

drugs, and the second hazard of adrenal cortical crisis postoperatively can be prevented by the judicious use of cortisone pre- and post-operatively.

Since both adrenals must be explored in operations for pheochrome tumors, a bilateral retroperitoneal approach is favored as the most direct and least traumatic. Some surgeons prefer a transabdominal approach; for if the tumor is extra-adrenal in location, it can be more readily located through an abdominal incision. Generally, however, presacral air studies will have excluded a retroperitoneal pheochromocytoma and the preoperative chest x-ray will have ruled out a thoracic pheochromocytoma. These studies are necessary to establish a definitive diagnosis.

### DIAGNOSTIC ADJUNCTS

The diagnostic adjuncts in studying patients with adrenal disturbances can be listed as follows: (1) Basal metabolic rate, $I^{131}$, or protein-bound iodine studies; (2) adrenolytic drugs—benzodioxane and regitine®; (3) intravenous pyelograms; (4) tolerance tests—water, glucose and DOCA; (5) blood chemistry—Na, K, glucose; (6) urinary hormonal measurements—17-ketosteroid, compound F and B; (7) presacral air injection; (8) lumbar aortography.

1. *Basal Metabolic Rate, $I^{131}$, or Protein-bound Iodine.* Pheochrome tumors of the adrenal may be mistaken for hyperthyroidism since the symptoms are suggestive and the basal metabolic rate may be elevated. The distinction can be made readily by the $I^{131}$ uptake of the thyroid gland or by a measure of the hormonal or protein-bound iodine. The $I^{131}$ uptake of the thyroid and protein-bound iodine of the blood are elevated in hyperthyroidism but not with pheochromocytoma.

2. *Adrenolytic Drugs.* The adrenolytic drugs are capable of blocking the transmission of sympathetic nerve impulses at the myoneural end-plate where epinephrine or nor-epinephrine may be the chemical transmitter of the nerve impulse. If given to patients with hypertension caused by a pheochrome tumor, a drop in blood pressure is generally produced. Contrariwise, if the hypertension is essential in origin, administration of an adrenolytic drug causes no change of an elevation of blood pressure since the drugs are also mild central nervous system stimulants. These tests are not infallible, but are a useful adjunct in the differential diagnosis of hypertension. The drugs most commonly used for this purpose are benzodioxane and regitine.

The test is carried out with the patient supine. A constant saline solution is given intravenously. Basal readings are obtained for twenty to thirty minutes. Benzodioxane, 10 mg. per square meter of body surface, are given in a 1 to 2 per cent saline solution, injecting it slowly over two minutes near the intravenous needle. Blood pressure readings are taken every minute thereafter until the blood pressure return to the pre-injection level.

The regitine test is conducted similarly but the dose is 0.33 mg./kg. intravenously.

Both benzodiozane and regitine have been used during the operation for pheochromocytoma to prevent hypertensive crises during surgery prior to removal of the medullary tumor. The dose is adjusted according to the need.

*Other drugs:* Histaine, .025 to 0.05 mg. intravenously, may produce a dramatic rise of blood pressure in cases of pheochromocytoma. Mecholyl, 10 to 25 mg. subcutaneously, has also been used to produce a similar reaction. These drugs are not as reliable and are more dangerous than the adrenolytic drugs since they elevate the pressure.

3. *Intravenous Pyelograms.* The presence of a suprarenal mass on the intravenous pyelograms or a displacement of the kidney are valuable diagnostic aids in patients with adrenal tumors. Unfortunately, unless the tumor is large it does not manifest itself readily, and normal pyelograms do not exclude adrenal disease.

4. *Tolerance Tests. Water:* The administration of a "water load" calls forth maximum activity of the adrenal steroids that have no oxygen at C-11. In Addison's disease diuresis is not promptly established; and this finding, in conjunction with inability to concentrate urea in the urine and to conserve chloride, is the basis of a special test called the Robinson-Kepler-Power water test. It is most widely used in testing for adrenal insufficiency, not hyperfunction.

*Salt:* The salt deprivation test is again used to test for adrenal insufficiency rather than hyperfunction. The patient takes less than 1.5 Gm. of salt per day with copious amounts of fluid for three days. In adrenal insufficiency

the urine still contains 50 to 100 mEq. of sodium or chloride, indicating failure to retain salt. It may be dangerous to perform if the patient has Addison's disease for it might precipitate an Addisonian crisis. It tests also for 11-desoxy corticoid function. It is called the Cutler-Power-Wilder salt deprivation test.

*Glucose:* This test is used to evaluate the activity of compounds oxygenated at C-11. The 11-oxy corticoids influence carbohydrate metabolism by decreasing peripheral utilization of glucose, increasing glycogen deposition in the liver and increasing the amount of glucose converted from protein. On the whole the 11-oxy corticoids have diabetogenic properties. Patients with Cushing's disease may have an elevated blood sugar and mild glycosuria, and this hyperglycemia tends to be insulin-resistant. The glucose tolerance curve in Cushing's disease tends to be of the diabetic type.

*5. Blood Chemistry. Potassium:* Patients with Cushing's disease commonly have an elevation of the carbon dioxide content of the plasma and a decrease in the plasma chloride and potassium. The plasma potassium loss is apparently the critical factor in this hypochloremic alkalosis, and reflects a total body loss of potassium in both the intracellular and extracellular fluids.

*Sodium:* Patients with Addison's disease commonly have a low serum sodium, but an elevation of serum sodium is not too frequent in Cushing's disease.

*Calcium and phosphorus:* In Cushing's disease the excretion of calcium in the urine is often excessive and osteoporosis is not uncommon. Negative calcium balances can occur even if the intake of calcium is high and the blood calcium normal.

*Glucose:* The blood glucose is often elevated in Cushing's disease. This is related to the decreased peripheral utilization of glucose and increased gluconeogenesis from protein. Actually the glycogen deposition in the liver is increased by the corticoids.

*6. Urinary Hormonal Measurements.* The urine contains a large number of steroids which are derived from the gonads and adrenals. The majority of urinary steroids have a keto group at C-17, and are called the 17-ketosteroids. Recently with improvements in chemical tests, corticoids (compounds E and F, the 11-oxycorticoids and desoxycorticoids) have been found and analyzed in the urine. Presumably the liver functions in the role of metabolizing or conjugating the steroids prior to excretion in the urine.

*Neutral 17-ketosteroids:* The neutral 17-ketosteroids come from two sources, the testis and adrenal cortex. Testosterone is the testicular precursor of many of these; corticosterone or cortisone may be the adrenal precursors of these 17-ketosteroids, or they may be derived from true androgenic hormones elaborated by the adrenal cortex. Interstitial cell tumors of the testes, masculinizing tumors of the ovaries, some cases of arrhenoblastoma and most cases of Cushing's syndrome have an increased excretion of urinary 17-ketosteroids (normal men $\pm 14$ mg./twenty-four hours; normal women 7 to 10 mg./twenty-four hours approximately). In Addison's disease the 17-ketosteroid excretion is low.

*Urinary corticosteroids:* The methods of urinary analysis for the 11-oxy steroids and the desoxycorticoids are still highly difficult, and too elaborate for routine clinical use. Nevertheless, in Addison's disease the values are lower than normal (11-oxy, .01 to .005 mg./twenty-four hours normally; desoxycorticosterone, .1 to .2 mg./twenty-four hours normally), and in Cushing's syndrome they are elevated. Easier and more reliable methods of analysis may be forthcoming soon, and will be a useful diagnostic adjunct.

*7. Presacral Air Injection.* Several years ago perirenal air insufflation was used in an effort to visualize the adrenals on x-ray examination. Unfortunately, an occasional exodus occurred from the examination, presumably from air embolism, and the procedure was generally abandoned. Recently similar studies have been accomplished in a large number of cases without incident by the technic of presacral injection.

The procedure is quite simple and can be performed with minimal premedication. With the patient lying on his side a finger is inserted into the rectum. A spinal needle is then inserted beneath the tip of the coccyx and guided into the retrorectal or anterior sacral space. Five hundred cubic centimeters of air is then injected with a syringe and gentle hand pressure, the patient lying first on one side and then the other. During the turning of the patient the needle can be removed and reinserted. The patient stands erect or lies with his head ele-

vated, and about two hours later films of the adrenal area are taken. The air rises in the retroperitoneal fatty tissue by gravity.

The procedure is a valuable diagnostic adjunct, but must be evaluated in association with other evidence since errors in interpretation occur.

8. *Lumbar Aortography*. Visualization of the adrenal blood supply and the adrenal glands can also be achieved by lumbar aortography. The procedure requires anesthesia, however, and carries some risk, probably approaching that of surgical exploration of the adrenals. It is of value only in an occasional special case at present.

### PRE- AND POSTOPERATIVE MEASURES

The problems in the management of patients undergoing adrenal surgery fall into two main categories: (1) those related to hypertensive crises and (2) those related to acute adrenal cortical insufficiency. The former category is seen in patients with pheochromocytoma prior to removal of the adrenal medullary tumor; the latter category is encountered in patients having subtotal or total adrenal resection for Cushing's syndrome, metastatic malignancy or essential hypertension. Acute postsurgical adrenal insufficiency is also troublesome in patients with marked hypopituitarism undergoing surgery or in patients who have been under prolonged cortisone suppression of the pituitary prior to surgery. The ability to increase temporarily the output of adrenal cortical steroids is an essential feature of the normal response to surgical stress.

*Presentation and Treatment of Hypertensive Crises.* The adrenolytic drugs, benzodioxane and regitine, have been used to control hypertensive crises prior to removal of an adrenal medullary tumor. They are best administered intravenously, the dose of benzodioxane being 10 to 20 mg. (10 mg. per square meter body surface) and regitine, 5 mg. After the tumor has been removed hypotension usually follows and nor-epinephrine may have to be utilized intravenously as necessary to maintain the blood pressure. The failure of the pressure to drop after an adrenal medullary tumor has been removed suggests that another pheochrome tumor is present either in the other adrenal or in an extra-adrenal location.

It must be emphasized that acute adrenal cortical insufficiency can follow surgery for adrenal medullary tumors, particularly if bilateral exploration with bilateral adrenal trauma has occurred. This is characterized by hypotension and fever with rapid collapse. Attempts to prevent this acute postoperative adrenal cortical insufficiency by the measures to be outlined should be followed.

TABLE III

| Schedule | Drugs Administered |
|---|---|
| Day before operation | 50 mg. cortisone acetate intramuscularly 4 times a day<br>5 mg. desoxycorticosterone acetate intramuscularly<br>5 gm. sodium chloride by mouth |
| Day of operation* | 150 mg. cortisone acetate at 7 A.M.<br>5 mg. desoxycorticosterone acetate at 7 A.M.<br>50 mg. cortisone acetate every 4 hours |
| First postoperative day | 50 mg. cortisone acetate intramuscularly every 6 hours<br>5 mg. desoxycorticosterone acetate intramuscularly<br>3 gm. sodium chloride by mouth |
| Second postoperative day | 50 mg. cortisone acetate 2 times a day<br>0 to 3 mg. desoxycorticosterone acetate as needed<br>3 gm. sodium chloride |
| Subsequent days | The dosage of steroids is gradually reduced until the sustaining dose of cortisone acetate (25 to 50 mg. daily) is reached about 1 wk. after operation; desoxycorticosterone acetate is not required for maintenance therapy |

* Operation performed at 8 A.M.; 500 cc. of 0.9 per cent sodium chloride and 500 cc. of plasma are injected intravenously during operation, and 10 μg. of nor-epinephrine per cc. are injected when systolic blood pressure falls below 100 mm.

*Prevention and Treatment of Acute Adrenal Cortical Insufficiency.* The standard method of pre- and postoperative management in patients with maximal adrenal cortical insufficiency, namely those with complete bilateral adrenalectomy, has been detailed by Huggins.[8] (Table III.)

Actually this schedule can be simplified and probably improved by the use of hydrocortisone intravenously on the day of operation and the addition of trimethylacetate of desoxycorticosterone after the first postoperative week. The need for extra salt and desoxycorti-

costerone acetate in the immediate postoperative period is not significant if adequate amounts of cortisone are administered. The present schedule follows that of Galante et al.[9] and has proved eminently satisfactory. (Table IV.)

TABLE IV

| Schedule | Drugs Administered |
|---|---|
| Day before operation | 100 mg. cortisone acetate |
| Day of operation: During operation | 100 mg. hydrocortisone in 1,000 cc. of 5 per cent dextrose saline |
| Postoperatively* | 100 mg. hydrocortisone in 1,000 cc. of 5 per cent dextrose in water<br>50 mg. hydrocortisone in 1,000 cc. of 5 per cent dextrose in water |
| First postoperative day | 25 mg. cortisone intramuscularly every 6 hr. Thereafter, if patient is tolerating oral feedings, 50 mg. cortisone acetate by mouth per day, with liberal salting of food† |
| Fifth postoperative day | 1 mg. desoxycorticosterone acetate intramuscularly daily; or 25 mg. trimethylacetate of desoxycorticosterone intramuscularly once every 21 to 30 days |

* Nor-epinephrine and blood are used as necessary to maintain blood pressure.

† Maintenance dose of cortisone acetate ranges between 25 to 50 mg. (37.5 mg. approx.) daily by mouth depending upon the patient's weight, insomnia and rounding of the face. Maintenance dose for desoxycorticosterone acetate and trimethylacetate of desoxycorticosterone are the same as those listed under fifth postoperative day.

It should be remembered that if an adrenal tumor is present, the opposite adrenal may have atrophied from excessive corticoid liberated by the tumor. The duration of administration of drugs postoperatively and the dosage schedule must, therefore, be dictated in part by the individual's needs rather than by hard and fast rules.

### SURGICAL CONSIDERATIONS

Two special considerations apply in influencing the method of approach to the adrenals in patients undergoing adrenal surgery: (1) the side of the lesion is unknown and both sides may have to be explored; and (2) tumors of the adrenal medulla may have an extra-adrenal location, generally in the retroperitoneal tissues. The adrenals can be approached transabdominally, retroperitoneally or transthoracically. The transthoracic approach is particularly suitable for large unilateral adrenal tumors, but it has the disadvantage that only one side can be visualized at a time. By opening the peritoneum intra-abdominal exploration can be accomplished through the transthoracic approach, and the other adrenal can be palpated as well as the retroperintoneal areas. However, only one side can be visualized, and it is for this reason that it is not recommended except for large unilateral lesions in which wide exposure is desired.

The transabdominal approach affords opportunity for bilateral adrenal and abdominal exploration simultaneously. It has been used satisfactorily by many surgeons, but is more difficult and traumatic than the subdiaphragmatic retroperitoneal approach. Through the abdominal exposure the kidney is palpated and above it the posterior peritoneum is opened over the adrenal. A unilateral subcostal incision can be used for one side, or a long transverse incision can be used to expose both sides simultaneously. The transabdominal approach permits easier exposure and removal of extra-adrenal retroperitoneal tumors, if one should be found.

Our own preference is for bilateral simultaneous exposure of the adrenals through retroperitoneal subdiaphragmatic incisions. This is more direct, less traumatic, and permits simultaneous observation of the glands and also fairly adequate retroperitoneal exploration if necessary. It is particularly valuable to employ this approach if one is performing simultaneous sympathectomy for hypertension. An incision is made over the twelfth rib, it is removed, the lumbodorsal fascia is opened, the retroperitoneal space entered subdiaphragmatically, and the adrenal is readily encountered and easily visualized. The patient is lying prone and an intratracheal tube is essential for safe airway during surgery. It is possible to open the peritoneum through this approach, but it is not often necessary if adequate preoperative studies have been performed.

*Bilateral Total Adrenalectomy for Advanced Carcinoma of the Breast.* The true role of total bilateral adrenalectomy in the management of

advanced carcinoma of the breast is still to be clarified. The largest experience with this therapy has recently been reviewed by Huggins and Dao[1] in their report of 100 cases. The operative mortality has been 5 per cent and no death has been attributed to postoperative adrenal crisis. Remissions of varying duration have occurred in 40 per cent of the cases, and although cure of cancer cannot be accomplished, noteworthy regression of cancer with marked alleviation of suffering has occurred in some patients for over three years. Fifty-five per cent of the patients were not improved by bilateral complete adrenalectomy. Whether or not one advises this type of therapy depends somewhat on one's surgical philosophy and how far one believes the surgeon is entitled to proceed in the alleviation of hopeless disease. Bilateral complete adrenalectomy is compatible with life only if the individual remains thereafter under fairly close medical observation with the opportunity for careful control of adrenal substitution therapy in the event of infection or stress. An Addisonian crisis can occur postoperatively at any time.

The rationale for the procedure is straightforward. Certain cancers are hormone-dependent in their growth characteristics. Cancer of the breast has long been known to be sustained by ovarian hormones. Huggins[10] demonstrated that there is also an adrenal component that sustains certain cancers of the breast. After removal of the gonads compensatory hypertrophy and increased function of the adrenal cortex occur. Therefore, in the removal of significant hormonal stimulus to breast cancer both the ovaries and adrenals must be removed completely.

To date the results have been most favorable if the following criteria are satisfied: (1) the patient should be over forty years of age but less than sixty-five; (2) the interval between radical mastectomy and the onset of recurrence should exceed two years; (3) the tumor should be fairly well differentiated histologically, and not of the duct-cell type; (4) the estrogen titre of the urine should be high, exceeding 10 I.U. per twenty-four hours; and (5) the remaining breast should show evidence of milk secretion on being challenged with luteotropin, 500 I.U. for seven days. These criteria are advocated by Huggins and Dao.[1]

*Bilateral Adrenalectomy in Essential Hypertension.* The association of hypertension with both Cushing's syndrome and pheochromocytoma of the adrenals, the development of hypotension in Addison's disease, and the peculiar interrelationships between salt retention, extracellular fluid volume and hypertension led to the employment of bilateral complete adrenalectomy for essential hypertension in man. Both the adrenal cortex and medulla are involved in the control of peripheral resistance, but they are not the sole factors, and again bilateral complete adrenalectomy is a palliative procedure in hypertension, not a cure.

The application of bilateral adrenalectomy to hypertension has been utilized in conjunction with sympathectomy by Jeffers et al.[11] With this technic a small amount, approximately 5 to 10 per cent of one adrenal gland, is allowed to remain. Thorn et al.[12] and Bowers[13] have employed bilateral complete adrenalectomy without sympathectomy. The results and indications in the two groups seem comparable enough so that the following conclusions may be drawn. The indications for the operation are essentially those for sympathectomy, namely: (1) malignant progressive hypertension that cannot be controlled by medical measures, including hypotensive drugs, and (2) chronic hypertension with marked organic changes. The operation seems contraindicated in patients with marked renal impairment but not in patients with congestive failure or marked retinal vascular changes. The patient should preferably be under fifty-five years of age and should be sufficiently cooperative and intelligent to take adrenal cortical replacement therapy postoperatively for life. Increased sodium and chloride loss is the most striking physiologic change following operation. Sudden stress, infection, or reduction of adrenal hormone therapy can precipitate an adrenal crisis hazardous to life at any time.

The initial results have been sufficiently encouraging to warrant further investigations of the procedure. However, with the passage of time it seems clear that the pressure may be lowered but the fundamental vascular disturbance continues, and ultimately these patients die from a complication of hypertensive cardiovascular disease. Initially significant drops in blood pressure are achieved in approximately 35 per cent of the cases and another 30 per cent may show a fair response to adrenalectomy.

SUMMARY

The adrenals occupy an interesting field for surgical study both from the specific disorders of the gland itself and from the possibilities of improving bodily functions through alteration of hormonal balances in disease.

The adrenal medulla elaborates two hormones, epinephrine and nor-epinephrine. Both hormones raise blood pressure, but epinephrine stimulates the pituitary-adrenal axis and decreases total peripheral resistance, whereas nor-epinephrine is vasoconstrictive through all vascular beds and does not affect pituitary-adrenal relations. Pheochrome tumors of the adrenal medulla produce both hormones, are characterized by paroxysmal or sustained hypertension with hypermetabolism, and offer problems of hypertensive crises and adrenal cortical insufficiency in their surgical removal.

The adrenal cortex elaborates several hormones related to salt and water metabolism, nitrogen metabolism, carbohydrate metabolism, adrenogenital functions and pituitary release of ACTH. Cushing's syndrome is the clinical picture of adrenal cortical tumors or hyperplasia, resulting in an increased production of corticoids. Virilism, feminism, or precocious sexual development may also result from adrenogenital hormones, an adrenogenital syndrome. Hypertension, abnormal body fat distribution and electrolyte disturbances are common in cortical tumors or hyperplasia.

The newest diagnostic adjuncts in the evaluation of abnormal adrenal states include the use of adrenolytic drugs, presacral air injection and urinary hormonal analyses.

Surgery of the adrenals requires attention to hypertensive crises during the operative procedure and avoidance of adrenal cortical insufficiency in the postoperative period. The adrenolytic drugs are useful in avoiding hypertensive crises. Cortisone, salt and DOCA in proper dosages can control postoperative adrenal cortical insufficiency and bilateral total adrenalectomy is now feasible with an operative mortality of 5 per cent.

Bilateral total adrenalectomy has been utilized to alter the hormonal environment in patients with hopeless breast carcinoma. Preferably the patient should be over forty-five, must have no residual ovarian hormonal activity, should have differentiated carcinoma with a fairly long interval between radical mastectomy and appearance of metastases. It is palliative, not curative, and is successful in about 35 per cent of the cases.

Extensive or total adrenalectomy has been utilized in the treatment of progressive malignant hypertension, with or without associated sympathectomy. Renal impairment is a contraindication to its use. It is again palliative in about 35 per cent of the cases, but does not cure the fundamental vascular disturbance in hypertension.

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# Surgical Treatment of Chronic Ulcerative Colitis

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CHRONIC ulcerative colitis is an intractable disease of unknown etiology that is not curable by medical treatment. The grave prognosis in this disease is evidenced in a report by Dennis[9] of a series of 102 patients treated medically, of whom over one-half ultimately died of the disease or some direct complication.

Chronic ulcerative colitis is curable by surgery. Such treatment is usually undertaken reluctantly because of the significant morbidity and mortality, and because of the problems of ileostomy care. The purpose of this paper is to review briefly the evolution of surgical treatment, and to present evidence that such treatment can now offer satisfactory prognosis for permanent cure and rehabilitation, with low morbidity and mortality rates.

Appendicostomy was advocated by Weir[19] in 1902 in order to provide a means of irrigation of the diseased colon with antiseptic solutions. This was considered an acceptable method of treatment during the next two decades, but ultimately the futility of such treatment lead to its abandonment.

Ileostomy then became the surgical treatment of choice. It was hoped that temporary diversion of the fecal stream might in time effect restoration of a normal healthy colon, so that the ileostomy could then be closed with resumption of normal bowel continuity and function. This proved to be a forlorn hope. Permanent diversion of the fecal stream did effect permanent remission of all symptoms of the disease in many patients. The high postoperative mortality of ileostomy was gradually lowered as the operation became less frequently a procedure of last resort in semi-moribund patients, and with better understanding of the control of fluid and electrolyte balance. (Table 1.) The development of the modern ileostomy bag, cemented to the skin to prevent fecal soiling, made possible the rehabilitation of the patient to a satisfactory economic and social life.

But ileostomy frequently failed to control such systemic complications of the disease as arthritis and cirrhosis, or the subsequent development of perforation, abscess, fistula or obstructing stricture. Warren and McKittrick[18] attributed 46 per cent of deaths following ileostomy to progression of the disease. Moreover, there has been increasing recognition of the fact that chronic ulcerative colitis predisposes to carcinoma, and that this threat to the patient's life continues, even though symptomatic remission of the disease has been achieved by ileostomy.[4] Bargen and his coauthors[2] have presented evidence that death from carcinoma of the rectum and colon among patients with chronic ulcerative colitis is thirty times as common as in the general population of the same age and sex. Counsell and Dukes[6] report an incidence of 11.1 per cent of carcinoma in sixty-three surgically treated patients. Their experience has shown also that the danger of carcinoma is greatly increased in those patients who have had colitis more than ten years. In all of their thirteen reported cases, carcinoma was unsuspected grossly, and these lesions were all anaplastic, exceptionally invasive, and showed unusually early lym-

TABLE 1
MORTALITY—ILEOSTOMY

| Author | Year | No. of Cases | Mortality (%) |
|---|---|---|---|
| Warren, McKittrick[18] | 1951 | 210 | 17.6 |
| Dennis, Karlson[9] | 1952 | 74 | 10.8 |
| Bacon, Trimpi[1] | 1953 | 36 | 11.1 |
| Cattel[5] | 1953 | 413 (prior 1947) | 18.0 |
| | | (since 1947) | 4.3 |
| Black, Sholl[3] | 1954 | 77 | 5.2 |

phatic spread. Other reports[2,9,12] have also shown that such carcinomas are rarely curable.

For these reasons, it is now generally accepted that adequate surgical treatment requires the removal of the diseased colon and rectum. The usual procedure has been that of a three-stage operation: ileostomy, followed after several weeks or several months by subtotal colectomy, and finally, after more weeks or months, by proctosigmoidectomy.

The rationale of ileostomy only as the first stage of surgical treatment has been based on the following premises: (1) the high morbidity and mortality following ileostomy contraindicated any additional surgical trauma with attendant additional risk, (2) restoration of physiologic fluid and electrolyte balance required a considerable period of time while the ileum accommodated itself to assuming the absorptive functions of the colon, and (3) regression of infection following diversion of the fecal stream decreased the risk of complicating infection at the time of colectomy.

Recently considerable doubt has arisen as to the correctness of these premises. Better knowledge of adequate control of fluid and electrolyte balance has decreased the mortality risk of ileostomy. Modern chemotherapeutic and antibiotic agents minimize the danger of complicating infection following primary resection of the diseased colon. Ileostomy alone does not immediately eradicate the systemic and local effects of the retained diseased colon. Miller, Ripstein and Tabah[13] have shown that ileostomy does not stop the serious loss of protein and blood from the diseased bowel. And finally, and most important, there appears to be a solution to the common and serious problem of ileostomy dysfunction, with time no factor in the ability of an unobstructed ileum to assume immediately the absorptive functions of the colon. The explanation of such dysfunction and the solution to the problem are credited to Turnbull.[16,17] He has shown that this is due to ileus caused by a severe serosal peritonitis on the surface of the protruding bowel. This can be avoided by a technic of primary suture of mucosa to skin at the time of creation of an ileostomy.

In 1949 Miller, Ripstein and Tabah[13] proposed that ileostomy and subtotal colectomy be performed simultaneously. (Table II.) Dennis[9] in 1952 reported that initial colectomy was repeatedly successful in critically ill patients, with far less postoperative morbidity than after ileostomy alone. Ripstein[15] in 1953 reported a series of 120 such operations with an operative mortality of 4.2 per cent. Forty-three of these patients were operated upon during acute exacerbation of disease, with an operative mortality in this group of 4.6 per cent.

TABLE II
MORTALITY
SIMULTANEOUS ILEOSTOMY AND SUBTOTAL COLECTOMY

| Author | Year | No. of Cases | Mortality (%) |
|---|---|---|---|
| Crile, Thomas;[7] Crile, Turnbull[8] | 1951 | 29 | 3.4 |
| Gardner, Miller[11] | 1951 | 69 | 4.4 |
| Dennis, Karlson[9] | 1952 | 30 | 3.3 |
| Ripstein[15] | 1953 | 120 | 4.2 |
| Bacon, Trimpi[1] | 1953 | 9 | 0.0 |
| Black, Sholl[3] | 1954 | 36 | 3.0 |

There are also a few recent reports of experience with single-stage resections of the entire colon and rectum with simultaneous ileostomy. (Table III.) This eliminates at the primary operation that portion of the large bowel which is usually most severely diseased. We believe that this should be the procedure of choice when surgical intervention is indicated in both the chronic and the acute phase of the disease. In support of this contention the following experience is cited.

TABLE III
MORTALITY
SIMULTANEOUS ILEOSTOMY AND COMPLETE PROCTOCOLECTOMY

| Author | Year | No. of Cases | Mortality (%) |
|---|---|---|---|
| Fallis, Barron[10] | 1953 | 2 | 0.0 |
| Palumbo, Rugtiv[14] | 1953 | 4 | 0.0 |
| Bacon, Trimpi[1] | 1953 | 5 | 0.0 |
| Black, Sholl[3] | 1954 | 28 | 3.2 |
| Author | 1954 | 19 | 0.0 |

### CLINICAL EXPERIENCE

During the past two years a total of twenty patients with chronic ulcerative colitis have been treated surgically on the author's private and clinic services at the Stanford University

Hospitals. Nineteen of these patients were treated by single-stage complete coloproctectomy and simultaneous ileostomy. One patient had a two-stage procedure of subtotal colectomy and simultaneous ileostomy, followed in seven weeks by abdominoperineal resection of the rectum and distal sigmoid. This seventeen year old girl was admitted to the hospital in critical condition, after she developed a large rectovaginal fistula and extensive cellulitis of the perineum and buttocks. She had been unable to retain any food for a period of four weeks and had marked nutritional edema. Serum protein totaled 3.7 mg. per cent, with A/G ratio of 1.4:2.3 mg. per cent. On the twelfth day of intensive medical treatment her general condition showed only slight improvement. She then developed an acute perforation and generalized peritonitis. Emergency surgery was performed in desperation. Generalized peritonitis and multiple perforations of involved distal ileum and sigmoid were found. The involved ileum and abdominal colon were removed to the mid-sigmoid and ileostomy established. Resection of the rectum was not done at the time, primarily because of the presence of an extensive perineal cellulitis. This was done seven weeks later, and the patient is now well. There were no deaths in the entire series.

In fourteen patients surgical treatment was an elective procedure for chronic debilitating disease. In six patients surgery was undertaken for acute toxic exacerbation of chronic disease uncontrolled by medical treatment after two to five weeks hospitalization.

### INDICATIONS FOR SURGERY

Complications of disease included pseudopolyposis in six patients; rectal stricture, five; nutritional edema, five; involved ileum, four; arthritis, three; skin lesions, three; ? carcinoma, two; hemorrhage, two; rectovaginal fistula, one and acute perforation, one.

Duration of symptoms prior to operation in these twenty patients averaged 6.7 years, ranging from nineteen months to eighteen years. Four of the twenty patients had had symptoms more than ten years.

The age of these patients at the time of operation ranged from thirteen to seventy years, the average being 35.4 years. Of the twenty patients in the group four were in their teens, four in the twenties, four in the thirties, four in the forties, two in the fifties, one in the sixties and one in the seventies.

The various forms of medical treatment employed prior to surgery in these patients is not relevant to this report. It is worthy of note that ten patients had had cortisone or ACTH or both, and seven had had psychotherapy.

TABLE IV
INCIDENCE OF ILEOSTOMY DYSFUNCTION

| Type of ileostomy | No. of Cases | No. with Dysfunction | Per cent |
|---|---|---|---|
| Long ileostomy (2 inches) | 5 | 5 | 100 |
| Long ileostomy with primary skin graft | 1 | 0 | 0 |
| Short ileostomy (1 inch) | 7 | 3 | 43 |
| Primary open ileocutaneous anastomosis | 3 | 0 | 0 |
| Turnbull technic of anastomosis | 4 | 0 | 0 |

*Postoperative Complications.* With one exception, which will be discussed later, there have been no instances of operative or postoperative shock in these patients. There have been no instances of cardiovascular or renal complications, or of peritonitis. The major problem has been that of ileostomy dysfunction. We are confident that there is a satisfactory solution to this problem, as evidenced by the fact that there has been no such dysfunction in the last seven patients in this series. The evolution of improved management of postoperative ileostomy dysfunction is demonstrated in Table IV. In the first five cases in this series 2 inches of ileum was brought up above the level of the skin and a soft rubber tube was inserted and fixed by purse-string suture of the end of the ileum. The tube was removed in three to six days. These patients all had prolonged periods of excessive discharge of watery green stool, interrupted by episodes of sudden diminution or cessation of fecal flow with symptoms and signs of intestinal obstruction relieved by reinsertion of a catheter through the ileostomy stoma. Some disturbance of fluid and electrolyte balance occurred during this period of ileostomy dysfunction but was readily controlled. It was evident that these difficulties were not the result of mechanical obstruction, but fitted in with Turnbull's explanation[16] that ileostomy dysfunction is the result of ileus caused by a

severe serosal peritonitis on the surface of the protruding bowel. Dysfunction continues during the "period of maturation" of the ileostomy, until ultimately the mucosa everts and approaches the skin.

Dysfunction was not a problem in one case in which a primary skin graft successfully eliminated the usual raw, infected serosal surface of the protruding ileum. However, in this instance, the resulting ileostomy stoma was so large that partial amputation was later required.

In the next seven patients a short ileostomy was devised in the hope that this would eliminate dysfunction. There was a definite decrease in the degree of dysfunction in this group, but three of the seven required reinsertion of a catheter for relief of obstructive symptoms. In the other four patients there was no recognized dysfunction, although by our present standards we now believe that a relatively long period of profuse watery ileostomy discharge was evidence of a minor degree of physiologic obstruction.

In the last seven patients, primary suture of the open end of the ileum to the skin was performed. No tube was inserted into the ileum at any time, and no digital dilatation of the ileostomy stoma was employed. In none of these seven patients was there evidence of any ileostomy dysfunction. Within three to five days the ileostomy discharge was a thick, mushy, yellowish brown stool, quite similar to the character of the fecal discharge which occurs with any long-standing, well functioning ileostomy. In three of these seven patients a simple primary open anastomosis of ileum to skin was accomplished with interrupted fine chromic catgut sutures. In the last four patients, Turnbull's technic of ileostomy was performed, with the added advantage of effecting a protrusion of the ileostomy stoma above the level of the skin thereby minimizing the problem of skin protection in the immediate postoperative period.

Successful management of ileostomy dysfunction has resulted in an appreciable shortening of the period of postoperative hospitalization. Patients with a long ileostomy were hospitalized for thirty-two days, those with a short ileostomy for twenty-two and a half days and those with a primary ileocutaneous anastomosis for sixteen and a half days.

Other postoperative complications in the nineteen patients who had a complete single-stage operation were as follows:

One patient, a man seventy years of age, went into profound shock two hours after operation was completed. More than adequate replacement of a minimal blood loss failed to counteract a progressive circulatory collapse. This patient had received large amounts of cortisone for many months for a severe arthritis, but had had none for four months prior to operation. In the belief that his reaction was due to acute adrenal insufficiency, intravenous hydrocortone was given for a period of five hours, together with intramuscular cortisone. Recovery was rapid and thereafter the postoperative course was entirely satisfactory.

Three patients were submitted to re-exploration for acute intestinal obstruction. In one of these patients a single inflammatory adhesion was obstructing the proximal ileum. In the other two patients diagnosis was in error, since no intra-abdominal obstruction or adhesion was found and the obstruction was relieved by insertion of a tube through the ileostomy.

In two patients strictures of the ileostomy stoma produced obstruction five and fourteen months after operation and required surgical correction. Neither of these patients had had primary ileocutaneous anastomosis.

In a number of patients skin irritation around the ileostomy was an annoying but not serious problem. In all patients the skin was in satisfactory condition before dismissal from the hospital to permit successful application of a Rutzen type ileostomy bag, cemented to the skin.

### SINGLE-STAGE COMPLETE PROCTOCOLECTOMY AN SIMULTADNEOUS ILEOSTOMY

*Preoperative Preparation.* Neomycin is the preferred antibiotic for antibacterial preparation of the bowel. In those patients who are able to tolerate food during the period of preoperative preparation, a non-residual diet high in protein and vitamins is given. Oral intake may have to be augmented by intravenous infusion of glucose, indicated electrolytes, salt-poor albumin, and whole blood. When the patient has received cortisone or ACTH, it is preferable to discontinue such treatment several days prior to operation. However, when either substance is the sole effective agent in suppressing the acute toxic symptoms of dis-

ease, it should be continued up to and following operation, with gradual withdrawal over a period of several days. Whenever the patient has received cortisone or ACTH in treatment of the disease at any time during the previous several months, the surgeon should be on the alert for possible adrenocortical deficiency shock in the immediate postoperative periods.

Gastric intubation and continuous suction is desirable for twelve hours prior to operation, so that the small intestine will be collapsed during operation.

*Operative Procedure.* Epidural anesthesia is preferred. A left paramedian incision from the pubis to 2 inches above the umbilicus is used. This permits adequate exposure and is well away from the selected site of ileostomy.

Mobilization of the entire abdominal colon is carried out from the cecum to the rectosigmoid. Mesenteric attachments and blood vessels are then ligated and divided.

The pelvic parietal peritoneum is then incised and the rectum mobilized down to the levators. Dissection is carried down close to the wall of the rectum, in order to preserve the nervi erigentes and avoid sexual impotence.

The rectosigmoid is then divided with a cautery between two hernia-tape ties. The distal rectal stump is encased in a rubber glove fixed by a hernia-tape tie. The pelvic parietal peritoneum is then closed to form a new pelvic floor. No peritonealization of the lateral gutters is done.

The site for transection of the ileum is now selected. This should be at least 6 inches proximal to the ileocecal valve, and at least 6 inches proximal to any involvement of the terminal ileum by disease. The site of the ileostomy stoma has been marked before the start of the operation, and is usually slightly less than halfway from the umbilicus to the anterior superior iliac spine. A circular excision of skin is made, with similar excision in the anterior rectus sheath, separation of rectus fibers, and simple incision in the posterior sheath and peritoneum, so that the opening just accepts two fingers. A Peyer clamp is then inserted through this incision and the ileum clamped. A second clamp is placed distal to the first and the ileum divided with a cautery. This completes the removal of the abdominal colon. The Peyer clamp is then withdrawn through the ileostomy incision so that 2 inches of ileum protrudes above the level of the skin. This is rotated to optimum position to avoid any twist in the mesentery. The edge of the mesentery immediately below the level of the peritoneum is then anchored for a distance of 1 inch to the anterior abdominal wall with several interrupted silk sutures. The peritoneal space lateral to the ileostomy spur is not closed.

The main incision is then closed, using interrupted steel wire mattress sutures in the anterior sheath.

Then the ileum is cut across with a scalpel against the blades of the Peyer clamp. The open end of the ileum is attached to the margin of the skin incision by interrupted sutures, preferably by the Turnbull technic.

Temporary dressings are applied and the patient turned in the jackknife position. The anus is closed with a purse-string suture of heavy braided silk and resection of the lower rectal stump is completed. The perineal wound is left open.

The patient is then replaced in the prone position and the temporary ileostomy bag applied. This is made from an ordinary refrigerator bag of small size, cutting a hole in the side of the bag the size of the ileostomy stoma. The bag is cemented to the abdominal wall with Paget dermatome glue, and a rubber tube is tied into the open end of the bag. This tube is extended over the side of the bed into a receptacle.

Between 1,000 cc. and 1,500 cc. of blood is usually administered during operation.

*Postoperative Treatment.* Gastric suction is discontinued and the tube removed at the completion of the operation. This may be resumed at a later time if regurgitation or vomiting develop.

Nothing is given by mouth postoperatively for twenty-four hours, then fluids are offered, and a high residue diet is given as soon as tolerated, usually in two to three days.

Daily intravenous infusions totaling 2,000 cc. are continued until there is adequate fluid intake by mouth. This is usually indicated for three to five days. If there is excessive fluid loss, this is replaced by additional infusions. Very seldom is it necessary to give more than 3,000 cc. in twenty-four hours.

Early ambulation is not forced, but permitted after the fifth day.

A stock ileostomy bag is applied after the third or fourth day. Measurements are taken

for permanent bags before the patient leaves the hospital.

## CONCLUSIONS

The surgical treatment of chronic ulcerative colitis can now offer satisfactory prognosis for permanent cure and rehabilitation of the patient, with low morbidity and mortality rates.

A single-stage surgical procedure of complete proctocolectomy and simultaneous ileostomy is recommended as the procedure of choice.

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# Treatment of Annular Pancreas

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THE embryologic origin of annular pancreas has been well discussed by previous writers.[1–6] The case reported herein consisted of marked dilatation of the proximal duodenum and of the well defined pancreatic tissue encircling the duodenum proximal to the ampulla of Vater. The duodenum was not greatly narrowed by the annulus and no obstruction of the lumen was observed.

The dilatation of the proximal duodenum could not be explained by an absence or paucity of the myenteric plexus since particular microscopic search showed numerous plexus elements. Duodenal ulceration just distal to the pylorus is the usual site for duodenal ulcer. The probable diagnosis of the case presented herein was made preoperatively by an alert radiologist. The x-ray findings are striking in the adult whose anatomic changes have been well established.

Roentgenologic examinations in newborns and infants are difficult because of the size of the patient, the upper intestinal tract obstruction and because of associated anomalies, such as atresia of the duodenum, congenital adhesions and malrotation of the gut.

Surgical treatment in reported cases has consisted of: (1) simple division or partial resection of the pancreatic ring; (2) joining the proximal dilated duodenum to distal duodenum or jejunum; or (3) gastroduodenostomy or gastrojejunostomy distal to the encircling pancreas, without excision of the dilated duodenum.

Incision or excision of the pancreatic ring has been followed by pancreatic fistulas, wound disruption, recurrence of symptoms, persistent dilatation of the duodenum and recurrent constriction. Most surgical successes have been after one of the bypassing procedures. The latter are especially advised for infants who require relief of obstruction in the most rapid manner with as little trauma as possible.

The operation employed in the patient reported herein removed the damaged duodenum, avoided a "blind loop" of the duodenum and restored the gastroduodenal continuity. It can only be used if the ampulla of Vater is distal to the pancreatic ring and if the duodenum distal to the pancreas is patent. Gastric resection was added to reduce the acid production of the stomach.

## CASE REPORT

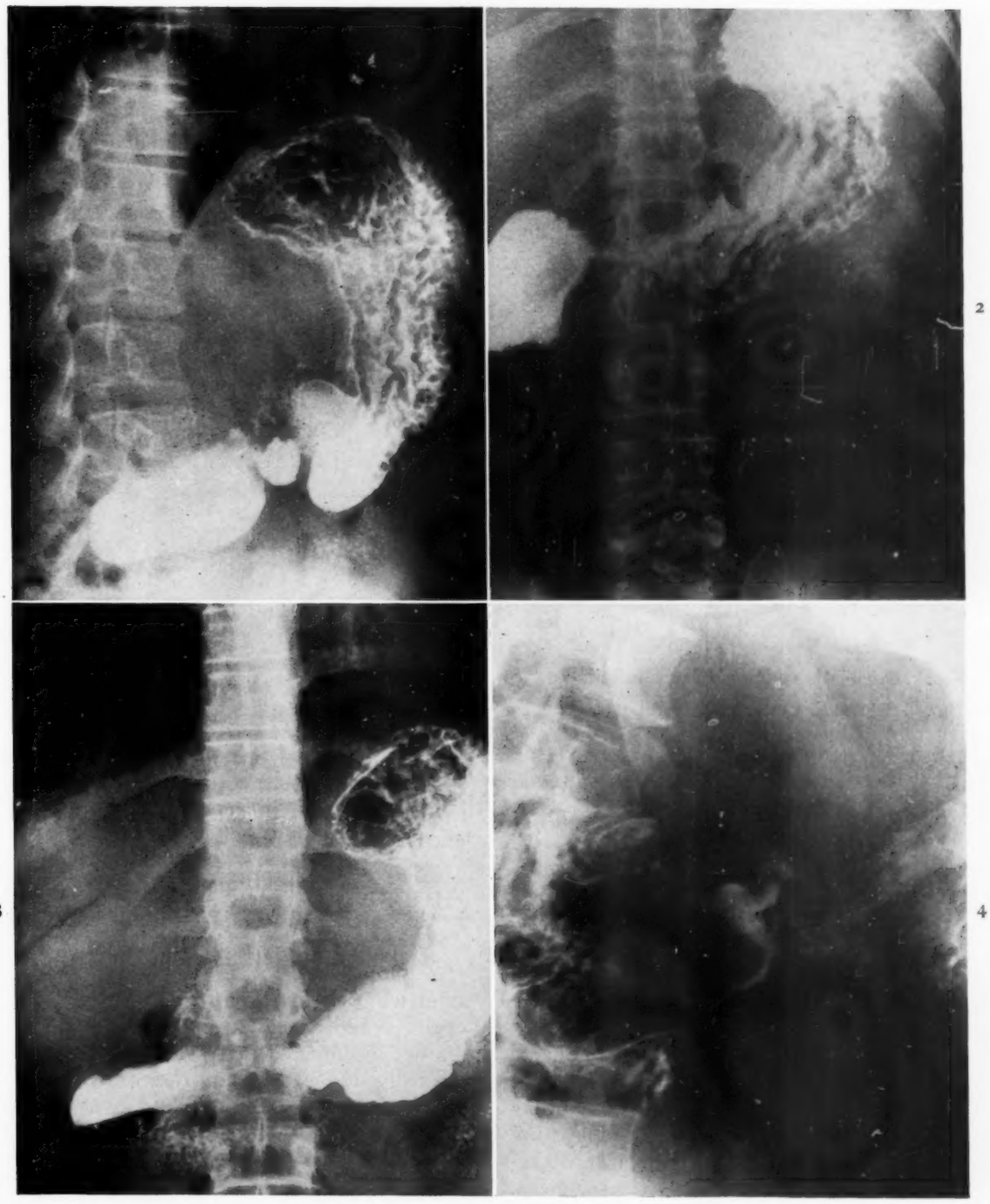
A white American businessman first noted epigastric distress and fullness for a few days at the age of twenty-seven. Six months later he experienced his second attack of upper abdominal distress which lasted a few days and disappeared without specific treatment. His third episode of acute indigestion occurred in June, 1952, when he was twenty-eight years old. He had just concluded a business trip involving air travel. Indigestion continued for over a week in the form of burning epigastric pain which often awakened him at night. He had discovered that ingestion of food or milk temporarily relieved his symptoms.

There had been no vomiting or change in bowel habits, and no weight loss. Until the age of twenty-seven he had had no symptoms of stomach or intestinal dysfunction. Neither college education nor his tour of duty in the Army during World War II had been interrupted by illness requiring hospitalization.

The examining physician found him to be well nourished with no abnormalities. Hemoglobin was 13.8 gm.; urine was normal and leukocytes were 8,100/cu. mm. Blood Wassermann was negative. Gastric juice titrated 46 degrees free HCl in the fasting specimen.

Gastrointestinal examination after a barium meal test demonstrated duodenal dilatation and partial obstruction, and a duodenal ulcer:

"Ingested barium shows the esophagus and stomach to be normal. Barium is easily expressed through a narrowed and deformed duodenal bulb which contains a tender ulcer crater. Just distal to the visible ulcer crater the duodenum immediately becomes extremely dilated forming a large pliable sac-like cavity



FIGS. 1 and 2. The first portion of the duodenum is markedly enlarged. Ulcer deformity is visible on the superior aspect of the dilatation, just distal to the cap in Figure 1.

FIG. 3. Part of the barium has been expressed from the dilated proximal duodenum back into stomach. Anterior projection of the duodenum proximal to the ring is well demonstrated.

FIG. 4. Barium remains in the ulcer crater of the duodenum distal to the cap.

into which the entire barium meal may be expressed from the stomach. With palpation in the reverse direction, the barium meal can be extruded in a retrograde direction into the stomach again. Only after this large cavity is filled with barium is any opaque material seen to pass downward through what would ordinarily be described as the second segment of the duodenum. After it passes this point, it travels rapidly through normal appearing second and third segments of the duodenum and into upper jejunum which is also normal in appearance."

"Multiple films confirm the fluoroscopic findings and show a normal appearing stomach, a deformed duodenal bulb containing a large ulcer crater, and the extremely dilated segment of duodenum between the ulcerated duodenal cap and what usually would be termed the second segment of the duodenum. This finding is interpreted as representing dilated duodenum proximal to some type of incomplete obstruction in the region of the head of the pancreas. There are several anatomical derangements which could be responsible for this partial obstruction: fibrous band crossing the second segment of duodenum, annular pancreas, aberrant vessel crossing the duodenum at this point, and congenital valve in the duodenum. (Figs. 1 to 4.)

Symptoms disappeared when the patient followed an ulcer diet regimen supplemented with banthīne,® 100 m.g every six hours. He readily accepted the explanation for his increasing indigestion and consented to surgical exploration on August 25, 1952.

At operation the stomach appeared normal. The first portion of the duodenum was approximately four to five times the normal diameter, thin-walled, flaccid, projecting anteriorly to conceal the annular ring of the pancreatic tissue situated just proximal to the ampulla of Vater. The pancreatic ring was approximately 1 cm. in width, less than 0.5 cm. in thickness on the anterior duodenal surface, widening to approximately a width of 2 cm. on the antero-lateral aspect of the duodenum after which it fused with the head of the pancreas. There was little constriction of the duodenal lumen by the pancreatic ring, for after division of the duodenum proximal to the ring a finger could be passed easily through the lumen surrounded by pancreas. Serosal stippling was seen on the anterior duodenal wall at the usual site for duodenal ulceration. In freeing the dilated duodenum no accessory pancreatic ducts were found. No bile duct or liver anomalies were demonstrated. (Fig. 5.)

The distal half of the stomach and the dilated duodenum were mobilized to the pancreatic ring. The duodenum was divided openly just proximal to the pancreatic constriction in order to demonstrate its patency. The ampulla of Vater was demonstrated distal to the

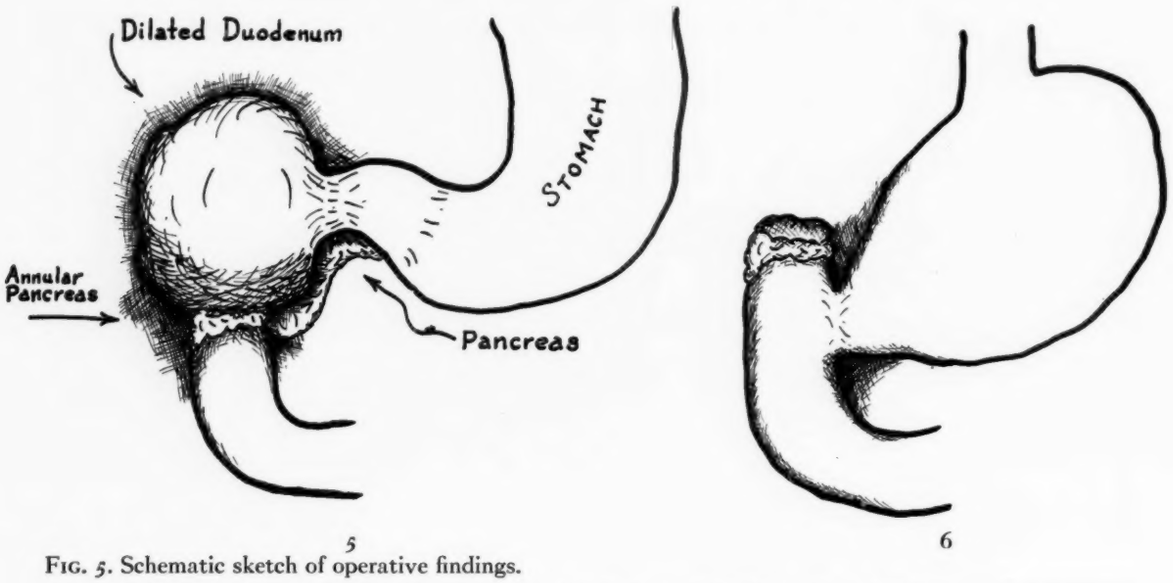



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FIG. 5. Schematic sketch of operative findings.

FIG. 6. Schematic sketch of subtotal gastric resection and gastroduodenostomy distal to annular pancreas.

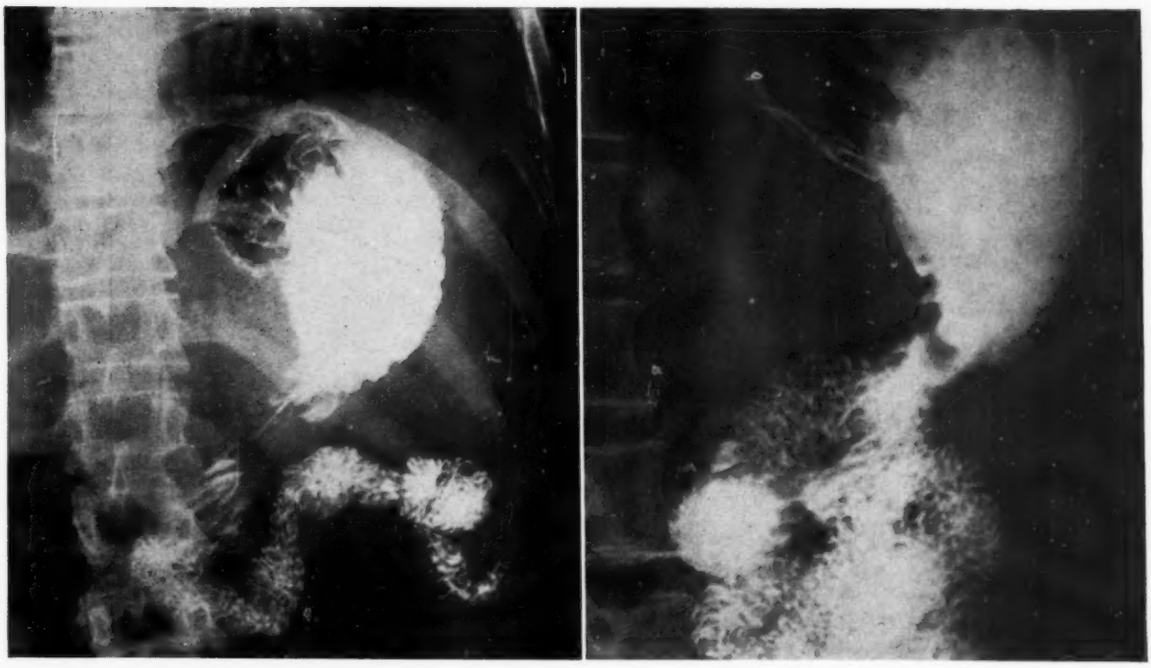

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FIG. 7. Gastrointestinal x-ray examination six weeks after surgery, showing functioning gastroduodenostomy.

FIG. 8. Gastrointestinal x-ray examination nineteen months after surgery. Rapid emptying of stomach through gastroduodenostomy.

annular band, and the duodenum then was closed using a Connell-type suture, reinforced with mattress sutures of fine cotton. The stomach was divided after the manner of Hofmeister uniting the greater curvature portion of the stomach to the duodenum below the annular pancreatic tissue. (Fig. 6.) The abdomen was closed without drainage. A nasogastric suction kept the stomach empty for two days, at which time liquid feedings were begun. The operative wound healed without event. He was dismissed from the hospital on the seventh postoperative day.

Microscopic study of the dilated duodenal segment showed diffuse fibrous thickening of the muscle and serosal layers. Myenteric plexuses were plentiful. There were areas of shallow erosion and ulceration of the mucosa. The microscopic diagnosis was: (1) stasis ulceration and hypertrophy, of the duodenal wall; (2) chronic gastritis, antrum stomach.

He returned to work approximately two weeks after the operation. An x-ray examination of his stomach six weeks after surgery showed a well functioning gastroduodenostomy. (Fig. 7.) Two months after operation he was permitted a normal diet. He reappeared nineteen months postoperatively following an intensive business trip during which he had had a few bouts of indigestion. Recently his diet had been irregular and unrestricted as is usual in the business world. He was smoking two packs of cigarettes daily.

Recheck gastrointestinal series in May, 1954, showed a well functioning gastroduodenostomy with an indentation of the duodenum where it had been closed above the annular ring. (Fig. 8.) His infrequent symptoms disappeared with home-cooked food at regular intervals, more attention to nightly rest and reduction of smoking.

SUMMARY

1. A case of duodenal obstruction and ulceration in association with annular pancreas in a twenty-eight year old man is reported.

2. Preoperative roentgen study demonstrated marked duodenal dilatation and partial obstruction. A presumptive diagnosis of annular pancreas was made.

3. No new etiologic factors were discovered for this anomaly.

4. Successful relief of the duodenal obstruction was achieved by removal of the dilated

duodenum, by subtotal gastric resection and by providing gastroduodenostomy distal to the pancreatic ring.

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# Surgical Treatment of Coarctation of the Aorta

## FURTHER EXPERIENCES WITH THE USE OF THE SUBCLAVIAN ARTERY

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AFTER Gross and Hufnagel's demonstration that the dog's descending thoracic aorta could be mobilized, temporarily occluded, and the ends re-sutured following excision of a small segment,[1] successful cases of excision of coarctation of the aorta with end-to-end aortic anastomosis were reported by Crafoord and Nylin[2] and by Gross.[3] Since then it has been evident to all that this is the ideal method of treatment. Occasionally, however, because of atypical location of the coarctation, rigidity of the aortic wall, unusual length of the area of coarctation, or the presence of an aneurysm, it is impossible to accomplish an end-to-end aortic suture. Such cases can be handled in a number of ways. The use of homologous aortic grafts has been shown to be practical,[4] and recent experiences make it evident that pliable plastic tubes are also satisfactory for aortic replacement.[5,6] In 1944 Blalock and Park had treated acutely made areas of aortic narrowing by end-to-side subclavian-aortic by-pass.[7] Shortly after the first successful operations for coarctation of the aorta were reported, the principle of Blalock and Park was applied in a number of cases by Clagett[8] and by Johnson and Kirby.[9]

In 1951 I reviewed briefly the recorded experiences with subclavian-aortic anastomosis, presented four personal cases, and made some suggestions concerning the use of the subclavian which it was believed would result in greater success.[10] Since the subclavian artery is invariably, or almost invariably, enlarged in cases of coarctation, it had been found that end-to-side anastomosis was unnecessary and that, instead, the subclavian could usually be sutured end-to-end to the distal aorta. Neither method, however, proved entirely successful since there resulted too high an incidence of unsatisfactory restitution of good aortic pathway and reduction in blood pressure. My own two experiences had been disappointing.

The first was a twenty year old man who was operated upon in May, 1948. Although his area of coarctation, which was situated at the base of the subclavian, was short, the aorta was so rigid that the end of the aorta could not be brought up for anastomosis to the base of the subclavian. The subclavian was divided at the level of its first branch and turned down. It, too, was so rigid it buckled much in the fashion of a bent lead pipe and it was obvious that this kinking would produce complete obstruction. An attempt was made to free the aortic arch more thoroughly with the hope that it could be depressed caudally sufficiently to permit anastomosis of the distal aorta to the base of the subclavian. Bleeding was encountered from a tiny rent in the aortic arch and eventually the patient was lost.

The second patient was a nearly fully grown girl of thirteen who was operated upon on January 4, 1950. The area of coarctation was situated just beneath the left carotid artery. The distal aorta could not be brought up to the base of the subclavian. The subclavian was transected, turned down, and an end-to-end subclavian-aortic anastomosis was carried out. The subclavian was pliable and there was no demonstrable kinking. An excellent pulsation was felt in the divided aorta. The good pulses present in the lower extremities during the first few days after operation disappeared on the fifth or sixth day, however, and have been weak or not palpable since. Blood pressure in the right arm prior to operation ranged from 140/80 to 180/110, and in the left arm from

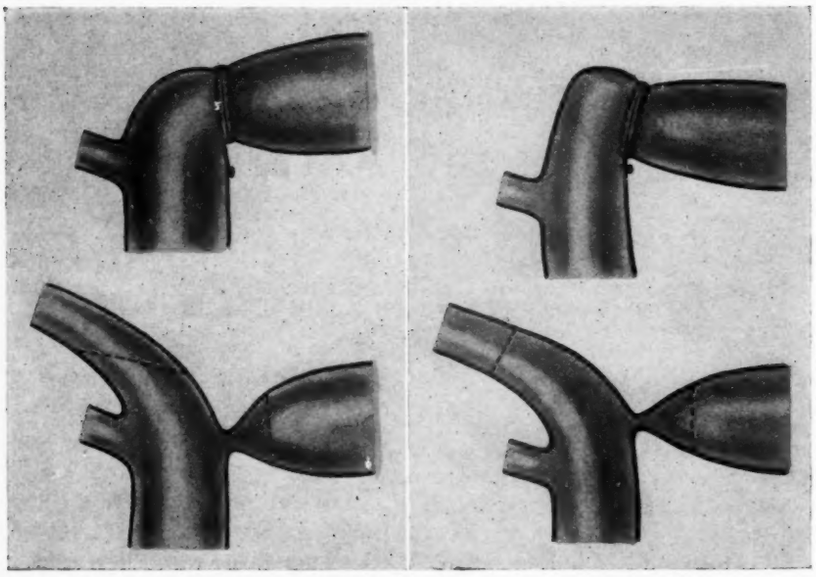

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FIG. 1. Sketch showing a modified method for end-to-end anastomosis of the subclavian artery and the distal aorta. The subclavian is divided in the plane of the long axis of the body rather than transecting it at a right angle.

FIG. 2. Drawing of a second modification of subclavian-aortic anastomosis. The subclavian is divided, clamped, held out in the axis of the aortic arch and depressed so an anastomosis can be accomplished between its base and the distal aorta. The excess portion of the subclavian is then amputated and closed by suture.

170/80 to 170/110. After operation blood pressure in the right arm was generally in the neighborhood of 140/85. In the hope of improving the situation the patient was re-explored in July, 1952, but the adhesions about the site of anastomosis were so dense and vascular the attempt was abandoned. Now, over four and a half years after the original operation, pulses in the femoral and posterior tibial arteries are only fair and the dorsal pedal pulses are very weak. Blood pressure in the right arm is 158/90 by auscultation, and 150 by palpation. Blood pressure in the right thigh is 120 by palpation.

Because of these difficulties no further efforts have been made simply to turn down a subclavian artery for end-to-end anastomosis with the distal aorta. In my earlier report one suggestion was made which entailed cutting across the subclavian artery tangentially in a plane more or less parallel to the long axis of the body rather than to transect it at a right angle. (Fig. 1.) This modification seemingly decreases the likelihood of buckling and permits one to have a large subclavian stoma for anastomosis. My original patient so treated has remained well. This eighteen year old man, operated upon on February 3, 1950, had a good result with restitution of excellent pulses, oscillometric values and blood pressure in the lower extremities and relief of hypertension. It would appear that this suggested maneuver would be useful in certain cases. I have had no further experience with it, however, for in the few cases in which it might have been applied, a second modification has been used instead.

The subclavian artery is ligated distally, clamped and divided. It is now held out in the axis of the arch of the aorta and depressed sufficiently to meet the end of the descending aorta. An opening of suitable size is made in the inferior aspect of the subclavian and side-to-end anastomosis with the aorta is then carried out. Following this procedure the remainder of the subclavian artery is amputated beyond the site of anastomosis and closed with the sutures. (Fig. 2.) My first patient treated in this manner, and reported previously, was operated upon in June, 1950. A good result was achieved with relief of hypertension and restitution of excellent pulses

to the abdominal aorta and the arteries of the lower extremities. Two additional patients have been treated in similar fashion.

### CASE REPORTS

CASE I. The patient was a nineteen year old male. Blood pressure in the right arm was 205/100 and in the right thigh 120/100. He was operated upon on April 15, 1953. The area of coarctation was situated at the base of the subclavian artery. When the descending aorta was divided from the area of coarctation, it retracted so markedly that in spite of adequate mobilization it was impossible to bring it up to the base of the subclavian for anastomosis. Utilizing the method described, an excellent anastomosis was accomplished. Convalescence was uneventful. At the time of discharge on the thirteenth postoperative day blood pressure was 150/70 in the right arm, 150/110 in the right thigh and 170/120 in the left thigh. Pulses were excellent in the abdominal aorta and in the lower extremities and oscillometric values were normal. When last seen, a year and a half after operation, the patient was asymptomatic and the pulses were excellent in the femoral, popliteal, dorsal pedal and posterior tibial arteries. Blood pressure in the right arm was 130/70 and in the right thigh 130/90.

CASE II. The patient was a twenty-one year old woman who complained of long-standing, rather marked weakness and fatigability, and of dyspnea on exercise. The blood pressure in the right arm was 230/90, in the right thigh 110/70. A very loud systolic and diastolic murmur was heard over most of the precordium but was loudest in the pulmonic area. On cardiac catheterization the catheter passed from the left pulmonary artery through a ductus into the descending aorta. Blood pressure in the left radial artery was 170/74.5, in the descending aorta and ductus 79/8, in the left pulmonary artery 78.5/45, and in the right ventricle 58.5/3. Electrocardiographic tracing showed a right bundle branch block and evidence suggestive of left ventricular hypertrophy, as well as premature ventricular systoles. Fluoroscopic and x-ray studies showed tremendous dilatation of the heart, definite enlargement of the right ventricle, left ventricle and left atrium. The pulmonary arteries were increased in size throughout the lung fields and pulsated actively. She was operated upon on August 25, 1954. The area of coarctation was most unusual: it was situated at the base of the arch of the aorta proximal to the point of origin of the carotid artery. (Fig. 3.) The major portion of it lay within the fibrous pericardium. The pulmonary artery was huge and communicated directly with the arch of the aorta through this area of coarctation. The descending aorta arose from a large ductus which came off the main pulmonary artery just below the point of union of the pulmonary artery and aorta. It was possible to divide the area of coarctation, close the openings in the arch of the aorta and main pulmonary artery, and to divide the ductus and suture its proximal end. The descending aorta was not long enough to permit its approximation to the base of the subclavian artery. Utilizing the technic described, a satisfactory anastomosis was carried out between the caudal portion of the divided and depressed subclavian artery and the descending aorta. The patient has done well. When seen last November the pulses in the lower extremities were excellent, the blood pressure in the right arm was 128/70 and in the right thigh 148/100.

These two modifications are applicable where the area of coarctation is at or near the base of the aorta or of the subclavian artery and where the gap between the descending aorta and the base of the subclavian, although too great to permit direct anastomosis, is relatively short. Excellent results have been obtained in the one case in which the first method was employed and in the three instances in which the second method was employed. Obviously neither method is applicable where there is a longer gap or in which the area of coarctation is situated at some distance below the base of the subclavian. In my original report the suggestion was made that the subclavian artery might successfully be used as a free autogenous graft. (Fig. 4.) It was thought that in cases in which the defect to be bridged was in the region of the first portion of the descending thoracic aorta, it might be possible to transect the subclavian artery at the point of its origin in a plane parallel to the long axis of the body and to re-suture the subclavian to the end of the arch of the aorta in such a way that it pointed caudally instead of in a cephalad direction. It was further suggested that under other circumstances a free graft of the subclavian

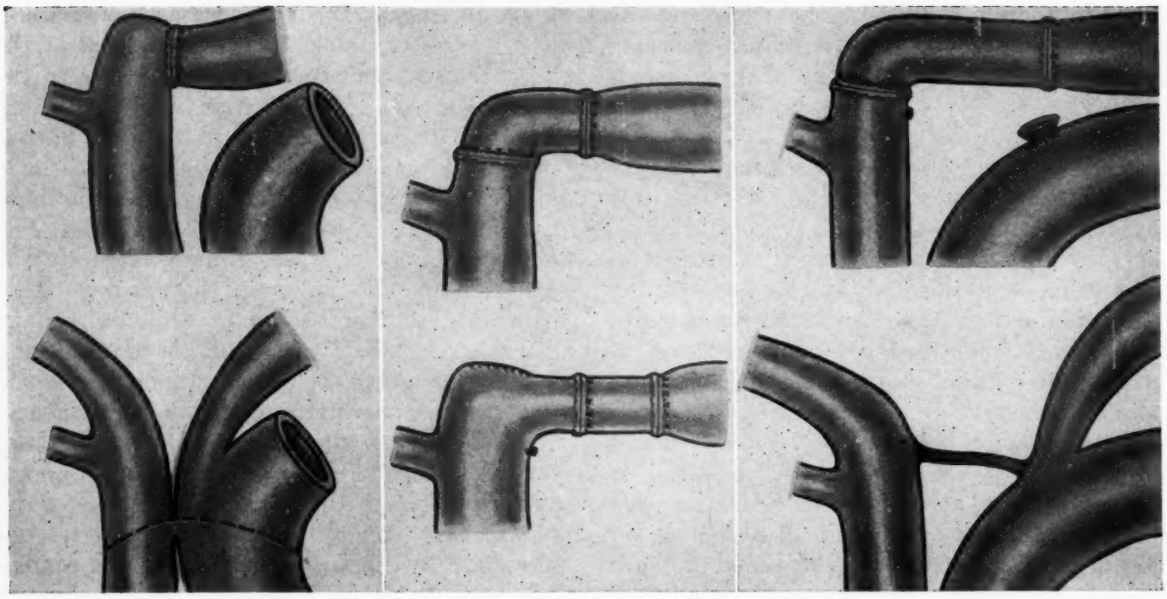

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FIG. 3. Drawing of findings encountered in Case II and the type of repair carried out. The interrupted line indicates line of attachment of pericardium to aorta and pulmonary artery.

FIG. 4. Drawings illustrating two possible methods for bridging aortic defect by use of subclavian artery as a free graft.

FIG. 5. Drawing showing anatomic situation in Case III and method of repair.

artery might be interpolated between the proximal and distal segments of the descending aorta. At the time of this report I had had no experience with this procedure. Subsequently on one occasion it has been used with success.

CASE III. The patient was a thirteen year old girl. Blood pressure in the upper extremities was 175/80 and in the lower extremities 100/80. She was thought to have, in addition to coarctation of the aorta, a patent ductus arteriosus because of the presence of a continuous murmur. She was operated upon on January 20, 1954. From the base of the subclavian a cord-like structure extended downward with an outside diameter of 3 mm. and about 2½ cm. in length. It joined the upper end of the lower segment of the descending aorta, which originated from the side of the left main pulmonary artery as a large patent ductus arteriosus. (Fig. 5.) It was obvious that some type of graft would be required. The long area of coarctation was divided; the ductus arteriosus was divided and its pulmonary end was closed with sutures. The subclavian artery was clamped and divided distally near the point of origin of the first branch. The distal end of the arch of the aorta was divided, the subclavian artery transected at its point of origin from the arch in a plane parallel to the long axis of the body and was re-sutured in such a fashion that it pointed downward instead of upward. The distal end was then easily sutured to the descending aorta. The patient had an uneventful convalescence and has had an excellent result. During the first eight months following operation she gained 27 pounds and grew considerably in height. When last seen pulses were excellent in the lower extremities, and blood pressure in the right arm was 120/80 and in the right thigh 124/90.

## COMMENTS

By now the total recorded experience with the operative treatment of coarctation of the aorta is considerable. It is universally agreed that the best method of treatment is excision of the area of coarctation and end-to-end restoration of continuity of the divided aorta, or, in case the area of coarctation is situated at the base of the aorta or the base of the subclavian, by division and anastomosis of the distal aortic segment to the base of the subclavian. It is equally apparent that such procedures are feasible in the majority of instances. Cases in which this ideal method of management are not applicable are encoun-

tered more commonly among older children and adults than among younger children. Careful extensive mobilization of the aorta, subclavian and distal end of the aortic arch often make it possible to accomplish this objective when on first inspection this seems impossible. On occasion, to be sure, the anastomotic stoma will not be quite as large as might be thought desirable. In my experience this compromise has not resulted in unsatisfactory restoration of a good aortic pathway or inadequate relief of hypertension. On occasion, however, such a direct restoration of aortic continuity cannot be achieved. Undoubtedly, some of these cases require the use of a preserved aortic graft or of an inert pliable plastic graft. A number of them, however, can be managed with success by use of the subclavian artery. My own small experience with simply turning down the subclavian artery for end-to-end anastomosis with the distal arterial segment, together with experiences recorded in the literature, make me loathe to utilize this procedure. The three modifications suggested in my earlier report and amplified in the present one provide methods which seemingly render the use of the subclavian artery extremely satisfactory. There are obvious advantages in restoring aortic continuity with autogenous tissues. These procedures are recommended for use in cases in which they are thought to be suitable.

*Addendum.* Since this paper was prepared a good aortic pathway has been restored in two additional cases by use of the subclavian artery as a free autogenous graft. One very ill child was treated at the age of seven months because of persistent unexplained fever, cough and difficult breathing. Blood cultures had been negative. Operation was carried out under moderate hypothermia on December 5, 1954. There were two areas of coarctation, one at the origin of the descending aorta and the other about 12 mm. distally. The intervening segment was only about 3 mm. in diameter. This was excised, the opening in the base of the aorta closed and the subclavian artery interposed as a graft in the same manner as was described in Case III. An excellent result was obtained. Preoperatively the blood pressure in the upper extremities varied from 160/80 to 190/100 and blood pressure was not obtained in the lower extremities. After operation there were excellent pulses in the abdominal aorta and the arteries of the lower extremities. Two and a half weeks after operation blood pressure in the arm was 120/85 and in the thigh 140/110. The fever persisted and by January 15th the left lobe of the liver was obviously enlarged. Exploration was carried out on that date and the tissue removed established the diagnosis of primary hepatoblastoma. The child died from this malignant lesion on February 10th. Postmortem examination revealed the graft to have healed well to the aortic arch above and to the descending aorta below, and to have provided an ample aortic pathway.

The second case was a very ill child nine months old. An open right atrial exploration on December 1st had failed to reveal previously diagnosed atrial septal defect. The child had a long-standing left upper lobe atelectasis and left lower lobe compensatory emphysema. These respiratory complications persisted as did evidence of cardiac failure. Operation was carried out under moderate hypothermia on December 18th. The area of coarctation was situated about 15 mm. below the arch. The proximal segment of the descending aorta was extremely small, having a diameter of only 2 or 3 mm. There was a small patent ductus communicating with the proximal segment. Because of hypoplasia the proximal segment was excised, and a segment of the left subclavian was interposed as a free graft between the base of the aortic arch and the distal segment of the descending aorta. The base of the subclavian was closed by suture. A good result was obtained and excellent pulses were immediately palpable in the arteries of the lower extremities. Unfortunately, the child continued to have marked respiratory difficulties and died a few days after operation. At postmortem examination there was passive congestion of liver, spleen and other organs, edema of the lungs, an ostium primum type of atrial septal defect 1 by 2 cm. in size, and a patent foramen ovale.

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# Aneurysm of the Hepatic Artery

## REPORT OF THREE CASES

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INSTANCES of aneurysm of the hepatic artery have been reported to a total of nearly 100 cases. Cumulative reviews[1–3,5,8,10] reiterate the difficulties of diagnosis and treatment. These publications and their bibliographies thoroughly present the historical background and the many scattered case reports of this lesion. It suffices here to summarize that the clinical diagnoses of hepatic artery aneurysm have been uncommon and successful surgical treatments even more rarely achieved. However, accumulated experience should by now prompt physicians to keep this aneurysm in mind as a possible cause for many cases of unexplained abdominal pain, obscure gastrointestinal hemorrhage or jaundice and of intra-abdominal or retroperitoneal hemorrhage. The purpose of this paper is to present three cases of hepatic artery aneurysm in which surgical exploration was done. In two of these cases a treatment apparently unreported specifically for this lesion has been satisfactorily applied.

The earliest of these cases, like many previously reported represents an instance in which the final answer to the problem of an acute abdominal hemorrhagic crisis was obtained only at autopsy.

### CASE REPORTS

CASE I. A sixty year old man with a known hypertension of 170/120 had complained of intermittent mild to moderately severe right upper quadrant discomfort for two years. Extensive studies, including full x-ray examinations, had failed to reveal a cause. On September 16, 1947, he was seized with a sudden, severe upper abdominal pain and was hospitalized. Examination of the abdomen revealed moderate upper abdominal tenderness, guarding to pressure, but no rebound or costovertebral angle tenderness. His blood pressure was 100/60, his temperature 99.4°F. The only positive laboratory finding was leukocytosis of 20,000 with 86 per cent polymorphonuclears, of which 27 per cent were immature. The rest of the blood count, sedimentation rate, urine, clotting time, serum amylase, blood urea and blood cholesterol and abdominal x-ray studies were normal. Within twenty-four hours the abdominal pain had become more severe. Increased guarding and rebound tenderness developed, along with a questionably palpable mass in the right upper quadrant. The findings upon laparotomy on September 17, 1947, were of a large quantity of fresh and clotted blood and a large retroperitoneal hematoma. After removal of the blood slight diffuse bleeding in the retroperitoneal space near the midline was noted, but no specific source could be found. When this oozing ceased with the temporary application of pressure, the abdomen was closed without further maneuvers. Postoperatively the blood loss was replaced; there was rapid improvement and the patient was eating well when dismissed on October 3rd. Three days later he again experienced sudden upper abdominal pain. He went into shock and, despite vigorous measures to treat the obvious hemorrhage, he died the same day. Autopsy revealed the bleeding point to be in a 2.0 cm. arteriosclerotic aneurysm of saccular form at the distal portion of the celiac artery but extending mostly onto the origin of the hepatic artery with rupture in the latter portion. In retrospect it is believed that definitive control of this aneurysm probably would have required ligation or an attempt at direct repair with re-enforcement.

The second case represents an aneurysm of the hepatic artery diagnosed only at the time of surgery.

CASE II. A forty-four year old man was hospitalized on August 3, 1950, with the chief complaint of severe epigastric pain of thirty hours' duration and of sudden onset. He gave

no history of indigestion, trauma, cardiovascular disease or of previous surgery. The patient's blood pressure was 140/80 and the positive physical findings were limited to the abdomen. The upper abdominal area was tense, guarded and tender to palpation. There was no back tenderness. Bowel sounds were heard only in the lower abdomen. No murmurs were noted. Routine laboratory examinations were normal, as was an x-ray film of the abdomen. Serum amylase studies were not available at that hour of the night. Within an hour the subjective pain became much worse; the upper abdominal tenderness and guarding increased notably. Under a tentative diagnosis of ulcer perforating into the lesser sac, pancreatitis or intra-abdominal bleeding, emergency laparotomy was performed. No peritonitis or bleeding could be found, but palpation deep to the stomach demonstrated a very strong arterial pulsation just to the right of the aorta associated with a striking systolic vascular thrill. Exploration through the gastrocolic omentum revealed a fusiform aneurysmal dilation of the proximal portion of the hepatic artery approximately 1.5 cm. in diameter and 3.0 cm. long. There was notable localized scarring about this swelling and marked edema of the adjacent pancreas and areolar tissue limited sharply to the area of the aneurysm. The vessel wall appeared to be extremely thin. In view of the fact that no bleeding had occurred from this vessel, the aneurysm was simply wrapped with reactive cellophane and the area was secondarily re-enforced with oxidized cellulose gauze. The patient's postoperative course was complicated by a small pulmonary embolus occurring before the calf tenderness was noted. He recovered uneventfully and had been working steadily when last seen early in 1954. He has had no further abdominal complaints of any sort. It has not been possible to obtain visualization studies of the abdominal vessels.

Case III. A twenty-three year old service station attendant was hospitalized on January 16, 1951, for the complaint of a steady, increasing epigastric pain which had appeared quite suddenly while he was lifting at his work. He described the pain as a steady one in the epigastrium without radiation. He had noted slight nausea several hours after the onset of pain, but no other symptoms. He gave no history of previous injuries, indigestion or previous surgery. About eight months before the onset of the present pain he had been examined by his physician on a suspicion of appendicitis with right lower quadrant discomfort. The record specifically notes that no abnormal abdominal sounds were heard with the stethoscope at that examination. Physical examination showed a normal blood pressure and pulse, and a temperature of 99.4°F. In the mid-epigastrium marked tenderness was elicited upon pressure with no radiation. Light palpation in this same area revealed a marked systolic thrill and auscultation demonstrated a loud, harsh systolic bruit. This could be heard over an area limited to about 6.0 cm. in diameter. Laboratory studies were within normal limits and abdominal films showed no abnormalities.

A preoperative diagnosis of intra-abdominal aneurysm was made, probably of traumatic origin and presumably involving either the hepatic or splenic artery. At laparotomy no signs of peritonitis or bleeding were found. Exploration through the gastrocolic omentum revealed a striking dilation of the proximal portion of the hepatic artery with a great deal of periarterial edema and mild thickening of the artery just distal to the aneurysm. A marked systolic thrill could be felt, and auscultation with a sterile stethoscope demonstrated the murmur noted preoperatively to be limited to the somewhat eccentric dilation of the artery. Treatment consisted of complete wrapping with polyethylene sheeting containing dicetyl phosphate and additional packing with gelatin foam pledgets. The patient made an uneventful recovery and has remained asymptomatic. By the second postoperative day the systolic murmur and palpable thrill had disappeared and have not recurred. An aortogram made about eighteen months after the operation demonstrated the celiac artery, the splenic and left gastric arteries, but showed no filling of the hepatic artery at its origin. It is presumed that gradual obliteration of the lumen may have taken place.

In Cases II and III the arterial wall showed a localized aneurysmal pulsation limited to a short area of the artery which was not present in any adjacent vessels nor at any point further along the hepatic artery. The perivascular edema and fibrosis was likewise limited. The treatment of this type of aneurysm is obviously not so difficult as in cases in which rupture has

occurred, so that the principle of re-enforcement and gradual occlusion, as has been earlier suggested,[4–6] was preferred to the unknown hazard of total ligation.

## COMMENTS

Of the several specific surgical treatments proposed for the treatment of hepatic artery aneurysm, ligation was the earliest applied and has again had recent success.[10] Except in the instances in which ligation is the only possible means of control, the high mortality ascribed to ligation of the hepatic artery has deterred many surgeons from employing this measure. Recent studies indicating a high degree of protection against fatal liver damage by the massive use of antibiotics may lead to greater safety in ligation. The safe ligation of the hepatic artery for the treatment of portal hypertension in cirrhosis must surely encounter a circulatory status markedly different from that to be found in the usual case of aneurysm.

An additional serious difficulty which may be encountered in the routine ligations is the existence of additional and inaccessible collateral vessels entering the aneurysm. Anomalies of this vascular distribution are common.[8] Collateral flow into an aneurysm was illustrated in a patient operated upon by Mathewson.[7] In this instance despite the closure of both ends of the aneurysm blood continued to flow from an opening in great quantity until ligation of the pancreaticoduodenal artery. This entered the sac and could be approached only after division of the body of the pancreas and rotation of the medial portion laterally. Failure to locate such additional vessels with a bleeding lesion would require such unsatisfactory measures as pack for control, but might be avoided in the unruptured aneurysm. Sampsel[11] reports such a problem.

In at least two cases[3,4] false aneurysms of the hepatic artery have been controlled by aneurysmorrhaphy with maintenance of the lumen. Such a procedure might have been feasible in our Case 1 had the opening been located. This treatment will suggest itself according to the nature of the aneurysm encountered. Splenic artery transfer has been used to augment circulation around an abdominal coarctation and to anastomose to the iliac artery, so that its use over a shorter course to the hepatic artery suggests itself. A recent application of intraluminal wiring[2] is an ingenious plan, although because of the small size of the entering vessels and the critical location of some aneurysms producing common duct obstructions this procedure will have limited application. It might be viewed with some caution if it were found to produce total immediate obliteration of the vessel. The recent popularity of vessel grafts suggests an attractive means of controlling these aneurysms, but the usual small size of the vessel and the frequency of arteriosclerosis will make this grafting difficult, except perhaps in some cases of trauma.

The diagnosis of unruptured aneurysms of the hepatic artery should be made with increasing frequency now that a greater awareness of the lesion is noted and diagnostic technics are available for visualization. The application of preoperative aortography is to be recommended if this is feasible for a particular patient. In four cases lesions suspected of being upper abdominal aneurysms have been proved to be otherwise by aortography. At the time of surgery the cause of a palpable thrill or localized systolic murmur had proved to be due to angulation or extrinsic pressure of the hepatic artery by tumor masses or the swelling of pancreatitis. The differentiation of hepatic artery aneurysms from those of the splenic artery is a valuable preoperative decision to be derived from contrast visualization. Although one is anxious to obtain the best possible distribution and high contrast in the vessels under study, it should be borne in mind that notable complications of translumbar aortography have arisen from the injection of the major volume of the medium in such a location as to permit large amounts in high concentration to damage either the renal or superior mesenteric circulation. For this reason it has been our practice to follow the contrast medium with several syringes of normal saline immediately after film exposure, in the hope that the low viscosity fluid will permit a more rapid dilution.

## SUMMARY

Three cases of aneurysm of the hepatic artery have been presented. In two instances successful control of unruptured aneurysms has been obtained by the application of irritant plastic sheet–wrapping of the aneurysm. Other methods employed or proposed are mentioned. A plea for more frequent search for this lesion

is made, especially with the application of aortography.

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# Author Index to Volume 89


Alway, R. H., 1138
Armada, O., 663
Artz, C. P., 773
Asbury, E., 719
Attinger, E., 387
Auerbach, O., 627

Bai, A. F., 331
Bailey, C. P., 272
Banyai, A. L., 383
Barach, A. L., 372
Barrett, R. J., 422
Bartone, N. F., 170
Bates, R. C., 1054
Beattie, E. J., 310
Beinfield, H. H., 957
Bell, L. G., 579
Beneventi, F. A., 1086
Bierman, H. R., 130
Björkman, S., 30
Bloomfield, A. L., 1109
Bobrowitz, I. D., 150
Bolton, H. E., 279
Boucot, K. R., 457
Bougas, J. A., 475
Boyden, E. A., 79
Boyes, J. H., 1116
Boynton, B. L., 924
Brackin, R. E., 872
Brantigan, O. C., 70
Brewer, L. A., 331
Briggs, J. N., 356
Bronwell, A. W., 773
Brown, G. D., 1099
Brown, J. B., 814
Brown, R. K., 745, 932
Bruce, N. E. T., 30
Bruwer, A. J., 1035
Buckner, H. T., 908
Byron, F. X., 356

Cahan, W. G., 494
Callahan, J. J., 908
Calman, C. M., 692
Campanale, R. P., 707
Campbell, D. A., 748
Campbell, J. A., 1009
Carlens, C. E. S., 30
Carothers, C. O., 879
Casberg, M. A., 721
Case, T. C., 935
Cavanagh, M. J., 707
Cave, E. F., 795
Chamberlain, J. M., 51, 673
Chandler, L. R., 1089
Childers, J. H., 1196
Christensen, N., 753
Close, H. P., 166
Cohn, R., 1120
Cole, J. P., 932
Connolly, J. E., 1123
Conte, A. J., 447
Coughlin, E. J., Jr., 875
Cracovaner, A. J., 211, 294
Craighead, C. C., 862
Creighton, F. S., 1086
Crenshaw, A. H., 879
Cullen, J. H., 687
Curry, G. J., 819

Da Costa, I. A., 1138
Davidson, L. R., 1042
Davis, E. W., 402
D'Esopo, N. D., 617
Dobson, L., 1128
Doherty, E. W., 1136
Domon, S. E., 995
Dorgan, J. A., 890
Dugan, D. J., 1023
Dziob, J. M., 745, 932

Edelstein, R., 583

Fox, C. L., Jr., 730
Friedman, L. L., 141
Fryer, M. P., 814

Garcia, A., 867
Gardner, C. McG., 725
Gelfand, M. L., 245
Gerbode, F., 1138
Gibbon, J. H., Jr., 484
Gittens, S. A., 986
Glas, W. W., 748
Gomila, F. R., Jr., 703
Goodman, J. M., 705
Grieco, R. V., 170
Gurd, F. N., 725
Gurdjian, E. S., 809
Guy, R. S., 1196

Haas, A., 573
Hackett, G. S., 968
Hadidian, C. Y., 70
Hale, H. W., Jr., 932
Hanbery, J. W., 1144
Hanson, H. E., 30
Hardaway, R. M., 583, 710
Hardin, C. A., 780
Hardy, K. L., 1023
Head, J. R., 1019
Heider, C. F., Jr., 964
Henderson, D. G., 968
Hertzler, J. H., 422
Hobby, A. W., 285
Hochberg, L. A., 425
Hodgson, C. H., 417
Hoffman, G., 550
Holman, C. W., 24
Holman, E., 1101
Howard, L. D., Jr., 1163
Hudson, W. A., 1

Ignatius, J., 753

Jackson, C. L., 319
Jacobson, L. F., 769
Jamison, W. L., 272, 279
Janes, H. H., 696
Janes, R. M., 297
Johnson, J., 56
Johnson, J. K., 1196
Johnson, P., 1169
Joseph, M., 608

Kane, I. J., 199, 324
Kaplan, I. W., 862
Karnofsky, D. A., 526
Katz, S., 402
Kiehn, C. L., 854
Kirby, C. K., 56

Lam, P. T. C., 593
Lamphier, T. A., 569
Lasker, S. E., 730
Lawrence, G. H., 795
L'Esperance, F. A., 717
Lewitan, A., 158
Lincoln, E. M., 645
Long, N. G., 569
Lord, J. W., Jr., 834
Losner, S., 158
Lundy, J. S., 35
Lyttle, S. N., 819

MacNeil, P., 569
Madding, G. F., 604
Mansfield, R. D., 759
Martin, F. A., 809
Martin, J. W., 1172
Martin, W. L., 700
Mathewson, C., Jr., 753, 1177

Mayer, E., 1002
McConville, B. E., 908
McDonald, J. R., 462
McKay, D. G., 583
McKay, D. R., 682
McKeown, J. J., Jr., 484
McLaughlin, C. W., Jr., 964
McLaughlin, H. L., 867
Meade, R. H., 1032
Meneely, G. R., 360
Mersheimer, W. L., 730
Mihaly, J. P., 986
Mitchell, R. S., 611
Mithoefer, J., 740
Moore, F. D., 1094
Motley, H. L., 106
Muri, J. W., 265
Murray, F., 465
Musselman, M. M., 748
Myers, W. P. L., 526

Naclerio, E. A., 16, 44
Nagel, G. W., 1182
Nathanson, L., 158
Neer, C. S., 11, 901
Nissen, R., 9
Noehren, T. H., 547

O'Brien, W. B., 663
O'Connor, H., 795
Orkin, L. A., 840
O'Rourke, P. V., 769
Ostrove, L. L., 600
Overholt, R. H., 475

Parker, E. F., 316
Parsons, H. G., 1187
Paulson, D. L., 347
Peabody, J. W., Jr., 402
Pearse, H. E., 1191
Pender, J. W., 35
Phillips, R., 526
Piel, J. J., 1138
Pittman, H. S., 974
Poppel, M. H., 439
Posch, J. L., 784
Poth, E. J., 1196
Potter, W. H., 932
Purdy, A., 1093, 1138
Puro, H. E., 1187
Putney, F. J., 304

Rao, K. V. S., 272, 279
Rappaport, I., 1002
Ravdin, I. S., 721
Rayport, M., 1144
Reich, N. E., 252
Reichert, F. L., 1203
Richards, V., 64, 1212
Ritter, S. A., 573
Ritvo, M., 470
Robinson, D. W., 780
Rogers, W. K., 995
Rosenberg, I., 1081
Roswit, B., 538
Rottino, A., 550
Rubin, M., 649
Rudman, I., 710

Sako, Y., 773
Saltzstein, H. C., 937
Samson, P. C., 364
Sass, R. E., 955
Scarborough, R. A., 1224
Schacter, B., 425
Schaer, S. M., 745
Schatten, W. E., 854
Schenk, W. G., Jr., 932
Schwartz, A. D., 1084
Sedgwick, C. E., 955
Segal, M. S., 387
Shaw, R. R., 347
Sherman, P., 692
Shidler, F. P., 1230
Shoemaker, W. C., 700
Shumacker, H. B., Jr., 1235
Siltzbach, L. E., 556
Silverstein, M. E., 730
Skerrett, P. V., 1081
Solow, A. L., 714
Spain, D. M., 118
Speed, K., 872
Stanley, A. L., 1054
Steelquist, J. H., 1241
Stein, J., 439
Steinberg, I., 215
Stiff, D. W. S., 932
Stokes, T. L., 484
Stone, P. W., 834
Storch, C. B., 188
Storey, C. F., 515
Stringer, C. J., 1054
Sugar, B., 1177
Summers, J. E., 1054
Swartley, R. N., 710

Taddeo, M. C., 696
Tartock, D. E., 583
Thompson, J. R., 637
Thorndike, A., 919
Trimble, H. G., 408
Tuttle, W. M., 422
Tysinger, D. S., Jr., 360

Uggla, L. G., 30

Valle, A. R., 90
Vandam, L. D., 101
Vindzberg, W. V., 663
Volk, B. W., 158
Voris, H. C., 803

Wagner, C. J., 911
Wahle, G. H., Jr., 583
Walske, B. R., 593
Warden, H. D., 579
Wasko, P. K., 712
Waterman, D. H., 995
Watson, W. L., 447
Webster, J. E., 809
White, P. D., 241
Wilson, N. J., 663
Winfield, J. M., 730
Wolf, M., 703
Woods, F. M., 979
Wrzesinski, J. T., 593

Yerushalmy, J., 231

# Subject Index to Volume 89

(E.) = Editorial


Abdominal injuries in Korea, 773

Abnormalities, air space, of lungs, 1002
Abscess of lung
  medical aspects of, 986
  medicosurgical problem, 995
Achilles tendon, injury to, 795
Acromioclavicular joint, repair of, 908
Adenocystoma lymphomatosum, papillary, 955
Adenomatosis, pulmonary, 515
Adrenals, surgery of, 1212
Agenesis of lung, 90
Air
  cysts, pulmonary, 1023
  space abnormalities of lungs, 1002
Alveolar cell tumor, 515
Amputees
  above-knee, suction socket prosthesis for, 919
  rehabilitation potential of, 924
Anastomosis, portacaval, and gastrointestinal hemorrhage, 1120
Anemia, chronic, hazard of transfusion in, 740
Anesthesiology in pulmonary surgery, 35
Aneurysm
  arteriovenous, of lung, 265
  of hepatic artery, 1241
  of temporal artery, 700
Angiocardiography in pulmonary disease, 215
Ankle as site of epiphyseal injuries, 879
Anomalies, developmental, of lungs, 79
Antibiotics and tuberculosis, 627
Antimicrobial agents in pulmonary tuberculosis, 617
Anus, hidradenoma of, 1081
Aorta, coarctation of, 1138, 1235
Appendectomy, Meckel's diverticulum and intussusception, 696
Appendicitis, acute, from gunshot trauma, 705
Arteriovenous
  aneurysm of lung, 265
  fistula, physiology of, 1101
Artery
  hepatic, aneurysm of, 1241
  subclavian, trauma to, 834
    use of in coarctation, 1235
  temporal, aneurysm of, 700
Atresia, bony, of posterior nares, 957
Avulsion, traumatic, of bladder neck and prostate complicating fractures of pelvis, 840

Back and disc problem in women (E.), 569

Bile
  duct rupture from trauma, 745
  peritonitis, 579
Biopsy, lung, for diagnosis of disseminated pulmonary disease, 166
Bladder neck and prostate, traumatic avulsion of, 840
Blebs, emphysematous, of lung, 1019
Bleeding, gastrointestinal, surgical significance of, 1177
Blood
  coagulation, altered, after incompatible blood transfusion, 583
  for extensive burns, 730
Bone, expendable, 819
Book reviews, 718, 1088
Bowel, large, injuries to, 753
Breast, carcinoma of (E.), 935
Brigham in Emile Holman's day, 1094
Bronchi
  segmental, and bronchopulmonary segments, 319
  surgery of, 331
Bronchiectasis, 979
  in the older patient, 974
  pulmonary resection for, 279
Bronchiolar carcinoma, 515
Bronchogenic carcinoma, 465
  preclinical, 457
  roentgen manifestations of, 470
Bronchography in pulmonary disease, 211
Bronchoplastic procedures, preservation of lung tissue by, 347
Bronchopulmonary
  disease, bronchoscopy in, 304
    diagnosis of, 141
    roentgen diagnosis of, 170
  segments, segmental bronchi in, 319
  sequestration, intralobar, 1035
Bronchoscopy in bronchopulmonary disease, 304
Bronchus, benign tumors of, 425
Bullae, emphysematous, of lung, 1019
Burns, extensive, treatment of, 730

Cancer
  of lung and primary cancer in other sites, 494
    and smoking, 447
  pulmonary, inoperable, primary and metastatic, 526
Carcinoma
  bronchiolar, 515
  bronchogenic, 457, 465
    roentgen manifestations of, 470
  of breast (E.), 935
  of lung, and surgery, 484
  pulmonary, detection, selection and resection in, 475
Cardiac
  and pulmonary diseases, differentiation between, 241

Cardiac arrest, 593
during pulmonary resection, 56
Catastrophes, major, surgical care in, 721
Cervix, anatomy of, 608
Chest
disease of, inhalational therapy in, 387
fluoroscopy of, 188
radiography of, in diagnosis of lesions, 231
Cholecystectomy, subtotal, in cholecystitis, 604
Cholecystitis and cholecystectomy, 604
Cholesterol granuloma, orbitofrontal, 1144
Cinemicrophotography in study of pial circulation, 809
Circulation, pial, and fatty emboli, 809
Clamp, non-crushing, for gastrointestinal surgery, 712
Clavicle and trauma to subclavian artery and vein, 834
Coagulation of blood, alterations in, 583
Coarctation of aorta, 1138
surgery for, 1235
Coin lesions, pulmonary, 408
surgery in, 422
Colitis, chronic ulcerative, surgery for, 1224
Commissurotomy
for mitral stenosis, 279
mitral, and pulmonary embolism, 272
Complications in pulmonary surgery, 70
Cough, pathology and management of, 285
Cyst
hydatid, of lung, 1042
of omentum, 710
pulmonary air, 1023
traumatic, of spleen, 1084
Cystic disease
infected, of lung, 1032
of lung, 1019
Cytology, pulmonary, 462

Decortication, pulmonary, surgical considerations in, 364
Defects of skull, repair of, 803
Diabetes, infection and gangrene of extremity in, 964
Diagnosis
anatomic location of neck tumor in, 937
and management of spontaneous pneumothorax, 360
of bronchopulmonary disease, 141
of disseminated pulmonary disease, 166
of lipoid pneumonia, 158
of pulmonary and heart disease, 252
of pulmonary carcinoma, 475
of pulmonary disease, radiography in, 199
of pulmonary lesions, radiography in, 231
of pulmonary tuberculosis, 611
of solitary circumscribed pulmonary lesions, 417
roentgen, in bronchopulmonary disease, 170
Diaphragm, acute injuries to, 769
Digital flexor tendon grafts, 1116
Disc and back problem in women (E.), 569
Disease
arteriosclerotic peripheral vascular, and gangrene, 600
bronchopulmonary, and bronchoscopy, 304
Disease, bronchopulmonary, diagnosis of, 141
roentgen differential diagnosis of, 170
cardiac and pulmonary, differentiation between, 241
cystic, of lung, 1019
heart and pulmonary, diagnosis of, 252
Hodgkin's, pathology of lung in, 550
infected cystic, of lung, 1032
of chest, inhalational therapy in, 387
pulmonary, and nose and throat, 294
and respiration, 106
and segmental localization, 324
angiocardiography in, 215
bronchography in, 211
effect of, on heart, 245
examination of sputum in, 150
lung biopsy in, 166
pathogenetic concepts of, 118
radioisotopes in, 538
respiration in, 106
surgery in, 1
Dislocation, posterior, of shoulder, 890
Disorders, pulmonary tension, in infants and children, 1009
Diverticulum, Meckel's, and intussusception, 696
Duct
bile, rupture of, from trauma, 745
common, strictures of, 1191

Edema, pulmonary, 310

Editorials
Critical analysis of treatment of carcinoma of breast, 935
Industrial disc and back problem in women, 569
Patient or a case, 1099
Presidential address, 719
Eggers' plates for fixation of femoral shaft fractures, 862
Emboli, fatty, and pial circulation, 809
Embolism, pulmonary, and mitral commissurotomy, 272
Emphysema
pneumoperitoneum in, 383
pulmonary, pressure and exsufflation in, 372
Epiphyseal injuries at ankle, 879
Exophthalmos, unilateral, from orbitofrontal cholesterol granuloma, 1144
Exsufflation in pulmonary emphysema, 372
Extractor, ureteral stone, complication from, 1086
Extremity
diabetic, infection and gangrene in, 964
lower, traumatic ulcers of, 854

Face, fractures of, 814

Femur
fractures of, 862
giant-cell tumor of, with metastasis, 573

Fistula
  arteriovenous, physiology of, 1101
  pulmonary arteriovenous, 1054
Fixation
  device for hip, 867
  two-plane, of femoral shaft fractures with Eggers' plates, 862
  wire, of facial fractures, 814
Fluoroscopy of chest, 188
Forceps, suturing, 717
Fractures
  of face, multiple interal wire fixation of, 814
  of femoral shaft, 862
  of head of radius, 911
  of pelvis, 840
  of tibia, 875
Function
  of pulmonary structures, 101
  tests in pulmonary surgery, 30

Gangrene
  and arteriosclerotic peripheral vascular disease, 600
  in diabetic extremity, 964
Gastric resection, 1136
Gastrointestinal
  bleeding, surgical significance of, 1177
  hemorrhage, massive, and portacaval anastomosis, 1120
Grafts
  digital flexor tendon, 1116
  embolic, in lungs of dogs, 1169
  fat pericardial, reinforcement with, 331
  skin, to palate, 692
Granuloma, orbitofrontal cholesterol, and unilateral exophthalmos, 1144
Gunshot trauma and acute appendicitis, 705

Hamartoma of lungs, 439
Hand, injuries to, 784
Head, atypical neuralgias of, 1203
Heart
  and pulmonary disease, diagnosis of, 252
  effect of pulmonary disease on, 245
Hemangioendothelioma of palate, 692
Hemorrhage
  massive gastrointestinal, and portacaval anastomosis, 1120
  pulmonary, 316
    in tuberculosis, 637
  treatment of shock from, 725
Hepatic injuries, 748
Hidradenoma of anus, 1081
Hip, fixation device for, 867
Hodgkin's disease, pathology of lung in, 550
Holman, Emile F., M.D., 1089
  and the Brigham, 1094
Humeral articulation, proximal, replacement of, 901
Hydatid cysts of lung, 1042
Hydrocele testis, rupture of, 703
Hysterectomy, total, 608

Infection in diabetic extremity, 964
Inhalation therapy for diseases of chest, 387
Injuries
  abdominal and thoracoabdominal, 773
  acute, to diaphragm, 769
  epiphyseal, at ankle, 879
  from corn picker, 780
  hepatic, 748
  to Achilles tendon, 795
  to hand in children, 784
  to large bowel, 753
  whiplash, complications of, 1203
Intussusception and invaginated Meckel's diverticulum, 696

Joint
  acromioclavicular, repair of, 908
  fusion and tomography, 872
  stabilization, 968

Leiomyosarcoma of rectum, 707
Lesions
  pulmonary coin, 408
    surgery in, 422
  pulmonary, diagnosis of, with radiography, 231
  solitary circumscribed pulmonary, diagnosis and management of, 417
Ligament proliferation for joint stabilization, 968
Ligation, visualization of iliac thrombophlebitis before, 1172
Localization, segmental, of pulmonary disease, 324
Lumbar sympathectomy in arteriosclerotic peripheral vascular disease with gangrene, 600
Lung
  abscess, a medicosurgical problem, 995
    medical aspects of, 986
  agenesis of, 90
  air space disorder of, 1002
  arteriovenous aneurysm of, 265
  benign tumors of, 425
  biopsy of, in disseminated pulmonary disease, 166
  cancer and primary cancer in other sites, 494
    and smoking, 447
  carcinoma of, and surgery, 484
  cystic disease of, 1019
  developmental anomalies of, 79
  hamartoma of, 439
  hematologic role of, 130
  hydatid cysts of, 1042
  infected cystic disease of, 1032
  of dog, embolic graft in, 1169
  pathology of, in Hodgkin's disease, 550

Lung, sarcoma of, 547
tissue, preservation of, 347
tumors, solitary, surgery of, 402

Meckel's diverticulum, invaginated, and intussusception, 696
Melanomas, prepubertal malignant, 1128
Metastasis, embolic, in prepuce of penis, 573
Migraine headaches, so-called, 1203
Mitral
commissurotomy and pulmonary embolism, 272
stenosis, commissurotomy for, 279
Muscle, skeletal, rhabdomyoma of, 1187

Nares, posterior, bony atresia of, 957

Neck, diagnosis of tumors of, 937
Neuralgias, atypical, of head, 1203
Nose and throat, relation of, to pulmonary diseases, 294
Nylon in repair of acromioclavicular joint, 908

Omentum, cyst of, 710

Open thorax procedure, surgical principles of, 51

Palate, hemangioendothelioma of, 692

Pancreas, annular, 1230
Pathology of lung in Hodgkin's disease, 550
Patient or a case (E.), 1099
Pedicled pericardial fat graft in tracheal and bronchial surgery, 331
Pelvis, fractures of, 840
Penis, embolic metastasis to, 573
Peptic ulcer, problems of, 1109
Peritonitis, bile, 579
Pial circulation and fatty emboli, 809
Plasma for extensive burns, 730
Pneumonia, lipoid, diagnosis of, 158
Pneumoperitoneum in emphysema, 383
Pneumotherapy for pulmonary tuberculosis, 687
Pneumothorax, spontaneous
diagnosis and management in, 360
treatment of, 356
Position, suspended prone, in pulmonary surgery, 44
Presidential address for The American Association for the Surgery of Trauma, 719
Pressure in pulmonary emphysema, 372
Proliferation of ligament for joint stabilization, 968
Prostate, traumatic avulsion of, 840
Prosthesis, suction socket, for above-knee amputees, 919
Pulmonary
adenomatosis, 515
air cysts, 1023
and cardiac diseases, differentiation between, 241
and heart disease, diagnosis of, 252
arteriovenous fistula, 1054
cancer, inoperable, primary and metastatic, 526
carcinoma, diagnosis and resection of, 475
Pulmonary, circulation, 130
coin lesions, medical and pathologic aspects of, 408
surgery in, 422
complications, postoperative, 297
cytology, 462
decortication, 364
disease and lung biopsy, 166
and nose and throat, 294
and segmental localization, 324
angiocardiography in, 215
bronchography in, 211
diagnosis of, with radiography, 199
effect of, on heart, 245
examination of sputum in, 150
pathogenetic concepts of, 118
radioisotopes in, 538
surgery in, 1
edema, 310
embolism and mitral commissurotomy, 272
emphysema, pressure and exsufflation in, 372
hemorrhage, 316
in tuberculosis, 637
lesions, diagnosis of, 231
solitary circumscribed, 417
resection and cardiac arrest, 56
and commissurotomy, 279
and open thorax procedure, 51
indications for, 16
principles of, 24
sarcoidosis, 556
structures, function of, 101
surgery, anesthesiology in, 35
complications in, 70
function tests in, 30
historical development of, 9
pre- and postoperative care in, 64
value of suspended prone position in, 44
tension disorders, roentgen manifestations of, 1009
tuberculosis and antimicrobial agents, 617
diagnosis of, 611
home management of, 682
pneumotherapy for, 687
resection for, 649
segmental resection for, 673
surgery for, 663
Pylorus, hypertrophic stenosis of, 1123

Radioisotopes in pulmonary disease, 538

Radius, fractures of head of, 911
Radiography in diagnosis of pulmonary disease, 199, 231
Rectum, leiomyosarcoma of, 707
Rehabilitation and re-employment potential of amputee, 924
Resection
for pulmonary tuberculosis in children, 649
gastric, 1136
of pulmonary carcinoma, 475

Resection, pulmonary, and cardiac arrest, 56
and open thorax procedure, 51
for bronchiectasis, 279
indications for, 16
principles of, 24
segmental, for pulmonary tuberculosis, 673
subtotal gastric, for peptic ulcer, 1182
Respiration, physiology of, in pulmonary disease, 106
Rhabdomyoma of skeletal muscle, 1187
Roentgen
differential diagnosis in bronchopulmonary disease, 170
manifestations of bronchogenic carcinoma, 470
of pulmonary tension disorders, 1009
Rupture
of hydrocele testis, 703
traumatic, of normal spleen, 759

Sarcoidosis, pulmonary, 556
Sarcoma of lung, 547
Segments, bronchopulmonary, and segmental bronchi, 319
Sequestration, intralobar bronchopulmonary, 1035
Shock, hemorrhagic, 725
Shoulder, dislocation of, 890
Sigmoidoscope for surgery, 714
Skin graft to palate, 692
Skull defects, repair of, 803
Sodium salt solutions for extensive burns, 730
Spleen
normal, traumatic rupture of, 759
traumatic cysts of, 1084
Spontaneous pneumothorax
diagnosis and management in, 360
treatment of, 356
Sputum, bacterial, examination of, in pulmonary disease, 150
Stenosis, hypertrophic pyloric, 1123
Stone extractor, ureteral, complication from, 1086
Strictures, common duct, vitallium tubes for, 1191
Suction socket prosthesis for above-knee amputees, 919
Surgery
for bony atresia of posterior nares, 957
for carcinoma of lung, 484
for chronic ulcerative colitis, 1224
for coarctation of aorta, 1138, 1235
for hemangioendothelioma of palate, 692
for pulmonary coin lesions, 422
for pulmonary tuberculosis, 663
for rheumatic tenosynovitis, 1163
gastrointestinal, non-crushing clamp for, 712
in major catastrophes, 721
in pulmonary disease, 1
of adrenals, 1212
of bronchi and trachea, 331
of tumors of lung, 402
principles of, in open thorax procedures, 51
pulmonary, anesthesiology in, 35
Surgery, pulmonary, complications in, 70
function tests in, 30
historical development of, 9
positions and approaches in, 44
pre- and postoperative care in, 64
sigmoidoscope in, 714
Suturing forceps, 717
Sympathectomy, lumbar, in arteriosclerotic peripheral vascular disease with gangrene, 600
Symposium on Bronchopulmonary Diseases
basic considerations, 285–309
bronchiectasis, abscess, cystic disease, 974–1053
coin lesions, 402–424
developmental anatomy, physiology and pathology, 79–140
diagnosis, 141–169
fundamental considerations in pulmonary surgery, 1–78
preservation of lung tissue, 331–355
pulmonary and cardiovascular systems, 241–279
decortication, 364–371
edema and hemorrhage, 310–318
emphysema and bronchial asthma, 372–387
segment, 319–330
roentgenology, 170–240
sarcoidosis, 556–568
spontaneous pneumothorax, 356–363
tuberculosis, 611–691
tumors, 425–555

Teaching by group consultation method, 932
Tendon
Achilles, injury to, 795
grafts, digital flexor, 1116
Tenosynovitis, rheumatic, surgery for, 1163
Testis, hydrocele, rupture of, 703
Thoracoabdominal injuries in Korea, 773
Thorax, open procedure for, 51
Throat and nose, relation of, to pulmonary diseases, 294
Thrombophlebitis, iliac, visualization before ligation, 1172
Tibia, complicated fractures of, 875
Tissue, lung, preservation of, 347
Tomogram after attempted joint fusion, 872
Trachea, surgery of, 331
Transfusion
in chronic anemia, 740
incompatible, and altered blood coagulation, 583
Trauma
and bile duct rupture, 745
cervical, complications of, 1203
conference, 932
gunshot, and appendicitis, 705
to subclavian artery and vein, 834
Tribute to Emile F. Holman, M.D., 1093
Tuberculosis
and antibiotics, 627
in children, treatment of, 645

Tuberculosis, pathology of, 627
pulmonary, and antimicrobial agents, 617
diagnosis of, 611
hemorrhage in, 637
home management of, 682
pneumotherapy for, 687
resection for, 649
segmental resection for, 673
surgery for, 663
Tubes, vitallium, for common duct strictures, 1191
Tumor
alveolar cell, 515
"benign," giant-cell, of femur, 573
of bronchus and lung, 425
of lung, surgery of, 402
of neck, anatomic location in diagnosis of, 937
Warthin's, 955

Ulcer
peptic, problems of, 1109
subtotal gastric resection for, 1182
traumatic, of lower extremities, 854
Ureteral stone extractor, complication from, 1086

Vascular replacements and reconstruction using inert material, 1196
Vein, subclavian, trauma to, 834
Vitallium tubes for common duct strictures, 1191

Warthin's tumor, 955

Whiplash injuries, complications of, 1203

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# Contents of Volume 89
## Scientific Papers


| | | |
|---|---|---|
| Surgery in Our Increasing Knowledge of Pulmonary Disease | *William A. Hudson* | 1 |
| Historical Development of Pulmonary Surgery | *Rudolf Nissen* | 9 |
| Indications for Pulmonary Resection | *Emil A. Naclerio* | 16 |
| Principles of Pulmonary Resection | *Cranston W. Holman* | 24 |
| Function Tests in Pulmonary Surgery | *Stig Björkman*, *N. E. Torsten Bruce*, *C. Eric S. Carlens*, *Hans Erik Hanson*, *Lars G. Uggla* | 30 |
| Anesthesiology in Pulmonary Surgery: Special Problems | *John W. Pender*, *John S. Lundy* | 35 |
| Operative Positions and Approaches in Pulmonary Surgery. Value of the Suspended Prone Position | *Emil A. Naclerio* | 44 |
| Surgical Principles Involved in Open Thorax Procedures. With Special Reference to Pulmonary Resection | *J. Maxwell Chamberlain* | 51 |
| Cardiac Arrest during Pulmonary Resection. Etiologic Factors and Management | *Julian Johnson*, *Charles K. Kirby* | 56 |
| Pre- and Postoperative Care in Pulmonary Surgery | *Victor Richards* | 64 |
| Complications Following Pulmonary Surgery | *O. C. Brantigan*, *C. Y. Hadidian* | 70 |
| Developmental Anomalies of the Lungs | *Edward A. Boyden* | 79 |
| Agenesis of the Lung | *A. R. Valle* | 90 |
| Some Observations on the Function of Pulmonary Structures | *Leroy D. Vandam* | 101 |
| Physiology of Respiration with Reference to Pulmonary Disease | *Hurley L. Motley* | 106 |
| Pathogenetic Concepts of Some Aspects of Pulmonary Disease | *David M. Spain* | 118 |
| The Hematologic Role of the Lung in Man | *Howard R. Bierman* | 130 |

| | | |
|---|---|---|
| Diagnosis of Bronchopulmonary Disease | *Louis L. Friedman* | 141 |
| Bacterial Examination of the Sputum in Pulmonary Disease | *I. D. Bobrowitz* | 150 |
| Diagnosis of Lipoid Pneumonia | *Bruno W. Volk*, *Samuel Losner*, *Alexander Lewitan*, *Louis Nathanson* | 158 |
| Lung Biopsy for the Diagnosis of Disseminated Pulmonary Disease | *Henry P. Close* | 166 |
| Problems in the Roentgen Differential Diagnosis of Bronchopulmonary Diseases | *Noel F. Bartone*, *R. Vincent Grieco* | 170 |
| Fluoroscopy of the Chest | *Charles B. Storch* | 188 |
| Current Radiographic Technics in the Diagnosis of Pulmonary Disease | *Irving J. Kane* | 199 |
| Bronchography in Pulmonary Disease | *Arthur J. Cracovaner* | 211 |
| Angiocardiography in Pulmonary Disease | *Israel Steinberg* | 215 |
| Reliability of Chest Radiography in the Diagnosis of Pulmonary Lesions | *J. Yerushalmy* | 231 |
| Clinical Differentiation between Cardiac and Pulmonary Diseases | *Paul D. White* | 241 |
| Effect of Chronic Pulmonary Disease on the Heart | *Maxwell L. Gelfand* | 245 |
| Pulmonary Diseases Secondary to Heart Diseases. Diagnosis and Treatment | *Nathaniel E. Reich* | 252 |
| Arteriovenous Aneurysm of the Lung | *Jan W. Muri* | 265 |
| Pulmonary Embolism Following Mitral Commissurotomy. With Special Reference to a Subvalvular Type | *W. L. Jamison*, *K. V. S. Rao*, *C. P. Bailey* | 272 |
| Simultaneous Pulmonary Resection for Bronchiectasis and Commissurotomy for Mitral Stenosis | *William L. Jamison*, *Houck R. Bolton*, *K. V. S. Rao* | 279 |
| Cough, Its Pathology and Management | *A. Worth Hobby* | 285 |
| Relation of the Nose and Throat to Pulmonary Diseases | *Arthur J. Cracovaner* | 294 |
| Postoperative Pulmonary Complications | *Robert M. Janes* | 297 |
| Bronchoscopy in the Diagnosis and Treatment of Bronchopulmonary Disease | *F. Johnson Putney* | 304 |

| | | |
|---|---|---|
| Pulmonary Edema | *E. J. Beattie* | 310 |
| Pulmonary Hemorrhage | *Edward F. Parker* | 316 |
| Segmental Bronchi and the Bronchopulmonary Segments | *Chevalier L. Jackson* | 319 |
| Segmental Localization of Pulmonary Disease. Medical and Surgical Significance | *Irving J. Kane* | 324 |
| Surgery of the Bronchi and Trachea. Experience with the Pedicled Pericardial Fat Graft Reinforcement | *Lyman A. Brewer*<br>*Angel F. Bai* | 331 |
| Preservation of Lung Tissue by Means of Bronchoplastic Procedures | *Donald L. Paulson*<br>*Robert R. Shaw* | 347 |
| Spontaneous Pneumothorax with Emphasis on Treatment | *John N. Briggs*<br>*Francis X. Byron* | 356 |
| Spontaneous Pneumothorax. Clinical Diagnosis and Management | *Donald S. Tysinger, Jr.*<br>*George R. Meneely* | 360 |
| Some Surgical Considerations in Pulmonary Decortication | *Paul C. Samson* | 364 |
| The Application of Pressure, Including Exsufflation, in Pulmonary Emphysema | *Alvan L. Barach* | 372 |
| Rationale of Pneumoperitoneum in the Treatment of Emphysema | *Andrew L. Banyai* | 383 |
| Advances in Inhalational Therapy in the Management of Diseases of the Chest | *Maurice S. Segal*<br>*Ernst Attinger* | 387 |
| Surgical Implications of Solitary Tumors of the Lung | *Edgar W. Davis*<br>*Sol Katz*<br>*J. Winthrop Peabody, Jr.* | 402 |
| Pulmonary "Coin" Lesions. Medical and Pathologic Aspects | *Harold Guyon Trimble* | 408 |
| Solitary Circumscribed Pulmonary Lesions. Diagnosis and Management | *Corrin H. Hodgson* | 417 |
| The Importance of Surgery in the Management of the Pulmonary Coin Lesion | *Wm. M. Tuttle*<br>*Raymond J. Barrett*<br>*J. H. Hertzler* | 422 |
| Benign Tumors of the Bronchus and Lung | *Lew A. Hochberg*<br>*Bernard Schacter* | 425 |
| Hamartoma of the Lungs | *Joseph Stein*<br>*Maxwell H. Poppel* | 439 |
| Lung Cancer and Smoking | *W. L. Watson*<br>*A. J. Conte* | 447 |

| | | |
|---|---|---|
| Preclinical Bronchogenic Carcinoma | *Katharine R. Boucot* | 457 |
| Pulmonary Cytology | *John R. McDonald* | 462 |
| Bronchogenic Carcinoma | *Foster Murray* | 465 |
| Roentgen Manifestations of Bronchiogenic Carcinoma | *Max Ritvo* | 470 |
| Detection, Selection and Resection in Pulmonary Carcinoma | *Richard H. Overholt*<br>*James A. Bougas* | 475 |
| Surgical Treatment of Carcinoma of the Lung | *John H. Gibbon, Jr.*<br>*T. Lane Stokes*<br>*John J. McKeown, Jr.* | 484 |
| Lung Cancer Associated with Cancer Primary in Other Sites | *William G. Caban* | 494 |
| Bronchiolar Carcinoma. (Alveolar Cell Tumor—Pulmonary Adenomatosis) | *Capt. Clifford F. Storey* | 515 |
| Treatment of the Inoperable Pulmonary Cancer, Primary and Metastatic | *David A. Karnofsky*<br>*W. P. Laird Myers*<br>*Ralph Phillips* | 526 |
| Radioisotope Therapy in Pulmonary Disease | *B. Roswit* | 538 |
| Sarcoma of the Lung | *Theodore H. Noebren* | 547 |
| Pathology of the Lung in Hodgkin's Disease | *A. Rottino*<br>*G. Hoffman* | 550 |
| Pulmonary Sarcoidosis | *Louis E. Siltzbach* | 556 |
| Industrial Disc and Back Problem in Women | *N. Gillmor Long*<br>*Timothy A. Lamphier*<br>*Phyllis MacNeil* | 569 |
| "Benign" Giant-cell Tumor of Femur with Embolic Metastasis in Prepuce of Penis | *Alfred Haas*<br>*Saul Alfred Ritter* | 573 |
| Bile Peritonitis | *Capt. Luther G. Bell*<br>*Comdr. Horace D. Warden* | 579 |
| Alterations in Blood Coagulation Mechanism after Incompatible Blood Transfusion. Clinical and Experimental Observations | *Capt. Donald G. McKay*<br>*Lt. Col. Robert M. Hardaway, III*<br>*Lieut. G. H. Wable, Jr.*<br>*Cpl. Richard Edelstein*<br>*Pvt. Donald E. Tartock* | 583 |
| Cardiac Arrest | *Pritchard T. C. Lam*<br>*John T. Wrzesinski*<br>*Benedict R. Walske* | 593 |

| | | |
|---|---|---|
| Evaluation of Lumbar Sympathectomy in Advanced Arteriosclerotic Peripheral Vascular Disease Complicated by Gangrene | *Lester L. Ostrove* | 600 |
| Subtotal Cholecystectomy in Acute Cholecystitis | *Gordon F. Madding* | 604 |
| New Concept of Total Hysterectomy and Anatomy of the Cervix | *Morris Joseph* | 608 |
| Diagnosis and Treatment of Pulmonary Tuberculosis | *Roger S. Mitchell* | 611 |
| Current Status of Antimicrobial Agents in the Treatment of Pulmonary Tuberculosis | *Nicholas D. D'Esopo* | 617 |
| Pathology of Tuberculosis As Affected by Antibiotics | *Oscar Auerbach* | 627 |
| Mechanisms of Fatal Pulmonary Hemorrhage in Tuberculosis | *J. Robert Thompson* | 637 |
| Indications for Treatment of Tuberculosis in Children | *Edith M. Lincoln* | 645 |
| The Role of Resection for Pulmonary Tuberculosis in Children and Adolescents | *Morris Rubin* | 649 |
| Surgical Treatment of Pulmonary Tuberculosis | *Norman J. Wilson*<br>*Orlando Armada*<br>*William B. O'Brien*<br>*William V. Vindzberg* | 663 |
| Segmental Resection for Pulmonary Tuberculosis | *J. Maxwell Chamberlain* | 673 |
| Home Management of Pulmonary Tuberculosis and Other Forms | *Donald R. McKay* | 682 |
| Present Status of Pneumotherapy in the Management of Pulmonary Tuberculosis | *James H. Cullen* | 687 |
| Hemangioendothelioma of Palate, with Wide Surgical Removal and Immediate Skin Graft | *Pincus Sherman*<br>*Clarence M. Calman* | 692 |
| Intussusception Due to Invaginated Meckel's Diverticulum after Previous Appendectomy | *M. C. Taddeo*<br>*H. H. Janes* | 696 |
| Temporal Artery Aneurysm | *William L. Martin*<br>*William C. Shoemaker* | 700 |
| Spontaneous Rupture of a Hydrocele Testis | *Monroe Wolf*<br>*F. R. Gomila, Jr.* | 703 |
| Acute Appendicitis from Gunshot Trauma | *Julien M. Goodman* | 705 |

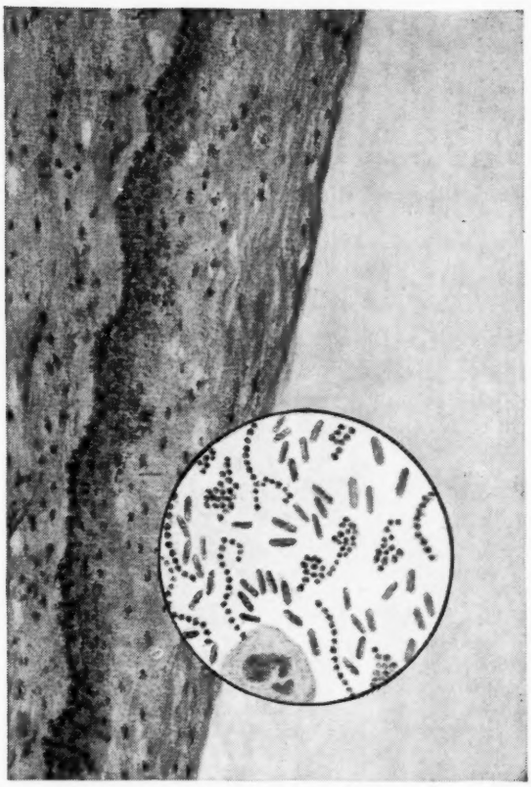
| | | |
|---|---|---|
| Leiomyosarcoma of the Rectum | *Lt. Col. Ralph P. Campanale*<br>*Michael J. Cavanagh* | 707 |
| Omental Cyst | *Lt. Col. Robert M. Hardaway, III*<br>*Capt. Robert N. Swartley*<br>*Capt. Irving Rudman* | 710 |
| A New Non-crushing Clamp for Gastrointestinal Surgery | *Peter K. Wasko* | 712 |
| An Improved Sigmoidoscope for Operative Work | *Alfred L. Solow* | 714 |
| A New Suturing Forceps | *F. A. L'Esperance* | 717 |
| Book Reviews | | 718 |
| The Breeding and Care of a Great Surgical Society | *Eslie Asbury* | 719 |
| A Second Look at Surgical Care in Major Catastrophes | *I. S. Ravdin*<br>*Melvin A. Casberg* | 721 |
| Reappraisal of the Treatment of Hemorrhagic Shock | *Fraser N. Gurd*<br>*Campbell McG. Gardner* | 725 |
| Observations on the Effects of Blood, Plasma and Sodium Salt Solutions in the Treatment of Extensive Burns | *Charles L. Fox, Jr.*<br>*Sigmund E. Lasker*<br>*James M. Winfield*<br>*Walter L. Mersheimer*<br>*Martin E. Silverstein* | 730 |
| The Hazard of Transfusion in Patients with Chronic Anemia | *James Mithoefer* | 740 |
| Bile Duct Rupture from External Blunt Trauma | *Sidney M. Schaer*<br>*Joseph M. Dziob*<br>*Roswell K. Brown* | 745 |
| Hepatic Injuries | *W. W. Glas*<br>*M. M. Musselman*<br>*D. A. Campbell* | 748 |
| Treatment of Injuries of the Large Bowel in Civilian Practice | *Norman Christensen*<br>*Joseph Ignatius*<br>*Carleton Mathewson, Jr.* | 753 |
| Traumatic Rupture of Normal Spleen | *Robert D. Mansfield* | 759 |
| Acute Injuries to the Diaphragm | *Paul V. O'Rourke*<br>*Lyle F. Jacobson* | 769 |
| Experiences in the Management of Abdominal and Thoracoabdominal Injuries in Korea | *Lt. Col. Curtis P. Artz*<br>*Capt. Alvin W. Bronwell*<br>*Capt. Yoshio Sako* | 773 |

| | | |
|---|---|---|
| Corn Picker Injuries | *David W. Robinson*<br>*Creighton A. Hardin* | 780 |
| Injuries to the Hand in Children | *Joseph L. Posch* | 784 |
| Injury to the Achilles Tendon. Experience at the Massachusetts General Hospital, 1900–1954 | *George Hugh Lawrence*<br>*Edwin F. Cave*<br>*Harrison O'Connor* | 795 |
| Repair of Skull Defects | *Harold C. Voris* | 803 |
| Response of the Pial Circulation to Fatty Emboli Studied by Cinemicrophotography | *J. E. Webster*<br>*F. A. Martin*<br>*E. S. Gurdjian* | 809 |
| Multiple Internal Wire Fixation of Facial Fractures | *Minot P. Fryer*<br>*James Barrett Brown* | 814 |
| Expendable Bone | *George J. Curry*<br>*Sydney N. Lyttle* | 819 |
| The Clavicle and Its Relation to Trauma to the Subclavian Artery and Vein | *Peter W. Stone*<br>*Jere W. Lord, Jr.* | 834 |
| Traumatic Avulsion of the Bladder Neck and Prostate Complicating Fractures of the Pelvis | *Lazarus A. Orkin* | 840 |
| Treatment of Traumatic Ulcers of the Lower Extremities | *Clifford L. Kiehn*<br>*William E. Schatten* | 854 |
| Two-plane Fixation of Fractures of the Femoral Shaft with Eggers' Plates | *I. W. Kaplan*<br>*C. C. Craighead* | 862 |
| Adjustable Fixation Device for the Hip | *Harrison L. McLaughlin*<br>*Alexander Garcia* | 867 |
| Use of the Tomogram after Attempted Joint Fusion | *Kellogg Speed*<br>*Roy E. Brackin* | 872 |
| Management of Complicated Tibial Fractures | *Edward J. Coughlin, Jr.* | 875 |
| Clinical Significance of a Classification of Epiphyseal Injuries at the Ankle | *Charles O. Carothers*<br>*Andrew H. Crenshaw* | 879 |
| Posterior Dislocation of the Shoulder | *Joseph A. Dorgan* | 890 |
| Indications for Replacement of the Proximal Humeral Articulation | *Charles S. Neer, II* | 901 |
| Repair of the Acromioclavicular Joint Using Nylon | *B. E. McConville*<br>*H. T. Buckner*<br>*J. J. Callahan* | 908 |
| Fractures of the Head of the Radius | *Carruth J. Wagner* | 911 |

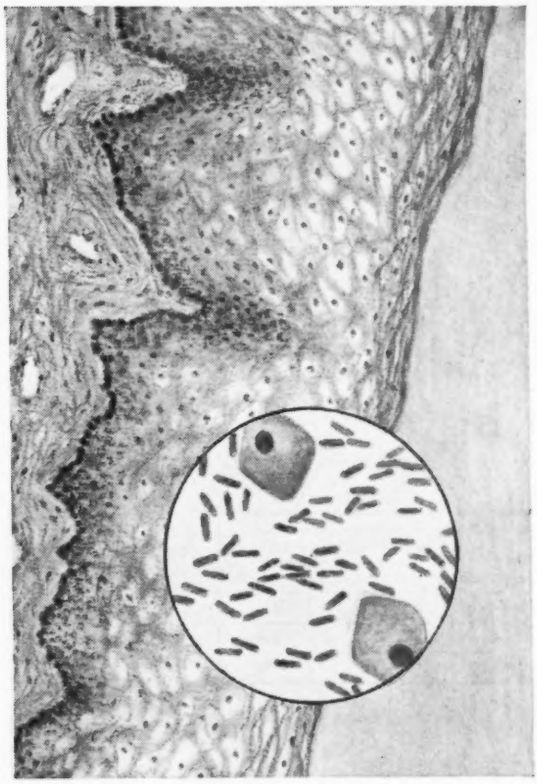
| | | |
|---|---|---|
| End Results in Suction Socket Prosthesis for Above-knee Amputees | *Augustus Thorndike* | 919 |
| The Rehabilitation and the Re-employment Potential of the Amputee | *Ben L. Boynton* | 924 |
| A Group Consultation Method of Teaching | *Roswell K. Brown*, *James P. Cole*, *Joseph M. Dziob*, *Harry W. Hale, Jr.*, *William H. Potter*, *Worthington G. Schenk, Jr.*, *Donald W. S. Stiff* | 932 |
| Officers of the American Association for the Surgery of Trauma, 1954–1955 | | 934 |
| A Critical Analysis of the Treatment of Carcinoma of the Breast | *Thomas C. Case* | 935 |
| Diagnosis of Tumors of the Neck. Especial Reference to Anatomic Location | *Harry C. Saltzstein* | 937 |
| Papillary Adenocystoma Lymphomatosum (Warthin's Tumor) | *Cornelius E. Sedgwick*, *Robert E. Sass* | 955 |
| Surgical Management of Complete and Incomplete Bony Atresia of the Posterior Nares (Choanae). With Detailed Description of an Improved Technic | *Henry H. Beinfield* | 957 |
| The Continuing Problem of Infection and Gangrene in the Diabetic Extremity | *Charles W. McLaughlin, Jr.*, *Charles F. Heider, Jr.* | 964 |
| Joint Stabilization. An Experimental, Histologic Study with Comments on the Clinical Application in Ligament Proliferation | *George S. Hackett*, *Donald G. Henderson* | 968 |
| Management of Bronchiectasis in the Older Patient | *Helen S. Pittman* | 974 |
| Bronchiectasis | *Francis M. Woods* | 979 |
| Acute Lung Abscess. With Emphasis on Medical Aspects | *S. Aubrey Gittens*, *John P. Mihaly* | 986 |
| Lung Abscess—A Medicosurgical Problem | *David H. Waterman*, *Sheldon E. Domm*, *William K. Rogers* | 995 |
| Air Space Abnormalities of the Lungs (Air Space Disorder) | *Israel Rappaport*, *Edgar Mayer* | 1002 |
| Roentgen Manifestations of Pulmonary Tension Disorders in Infants and Children | *John A. Campbell* | 1009 |

| | | |
|---|---|---|
| Cystic Disease of the Lung. With Emphasis on Emphysematous Blebs and Bullae | *Jerome R. Head* | 1019 |
| Pulmonary Air Cysts—A Therapeutic Concept | *David J. Dugan*<br>*Kenneth L. Hardy* | 1023 |
| Infected Cystic Disease of the Lung | *Richard H. Meade* | 1032 |
| Intralobar Bronchopulmonary Sequestration | *Andre J. Bruwer* | 1035 |
| Hydatid Cysts of the Lung | *Louis R. Davidson* | 1042 |
| Pulmonary Arteriovenous Fistula | *Christopher J. Stringer*<br>*Arthur L. Stanley*<br>*Richard C. Bates*<br>*John E. Summers* | 1054 |
| Hidradenoma of the Anus | *Irving Rosenberg*<br>*Philip V. Skerrett* | 1081 |
| Traumatic Cyst of the Spleen | *A. David Schwartz* | 1084 |
| Complication Following the Use of a Ureteral Stone Extractor | *Francis A. Beneventi*<br>*Francis S. Creighton* | 1086 |
| Book Reviews | | 1088 |
| Emile F. Holman, M.D. | *Loren R. Chandler* | 1089 |
| A Tribute | *Ann Purdy* | 1093 |
| The Brigham in Emile Holman's Day | *Francis D. Moore* | 1094 |
| A Patient or a Case | *George D. Brown* | 1099 |
| The Physiology of an Arteriovenous Fistula | *Emile Holman* | 1101 |
| Some Problems of Peptic Ulcer | *Arthur L. Bloomfield* | 1109 |
| Evaluation of Results of Digital Flexor Tendon Grafts | *Joseph H. Boyes* | 1116 |
| Massive Gastrointestinal Hemorrhage in the Presence of Portacaval Anastomosis | *Roy Cohn* | 1120 |
| Hypertrophic Pyloric Stenosis in the Adult | *John E. Connolly* | 1123 |
| Prepubertal Malignant Melanomas. Report of Two Cases | *Leonard Dobson* | 1128 |
| Gastric Resection. A Compilation of Technics | *Edward W. Doherty* | 1136 |
| Surgical Treatment of Coarctation of the Aorta in Infancy. Report of Two Cases | *Frank Gerbode*<br>*Ann Purdy*<br>*Robert H. Alway*<br>*John J. Piel*<br>*Iseu Affonso Da Costa* | 1138 |

| | | |
|---|---|---|
| Unilateral Exophthalmos Due to Orbitofrontal Cholesterol Granuloma | *John W. Hanbery*<br>*Mark Rayport* | 1144 |
| Surgical Treatment of Rheumatic Tenosynovitis | *Lot D. Howard, Jr.* | 1163 |
| Embolic Grafts in the Lungs of Dogs | *Phillips Johnson* | 1169 |
| Iliac Thrombophlebitis—Visualization Prior to Ligation. Case Report | *James W. Martin* | 1172 |
| Surgical Significance of Gastrointestinal Bleeding | *Carleton Mathewson, Jr.*<br>*Benjamin Sugar* | 1177 |
| Subtotal Gastric Resection for Peptic Ulcer. Historical Review with the Description of a Variation in Technic | *Gunther W. Nagel* | 1182 |
| Rhabdomyoma of Skeletal Muscle. Report of a Case | *Harry G. Parsons*<br>*Henry E. Puro* | 1187 |
| End Result of Using Vitallium Tubes in Common Duct Strictures | *Herman E. Pearse* | 1191 |
| Vascular Replacements and Reconstruction Utilizing Inert Material | *Edgar J. Poth*<br>*John H. Childers*<br>*Joseph K. Johnson*<br>*Robert S. Guy* | 1196 |
| Atypical Neuralgias of the Head. Headaches, So-called Migraine and Complications of Whiplash Injuries and Other Cervical Trauma | *Frederick Leet Reichert* | 1203 |
| Surgery of the Adrenals | *Victor Richards* | 1212 |
| Surgical Treatment of Chronic Ulcerative Colitis | *Robert A. Scarborough* | 1224 |
| Treatment of Annular Pancreas | *Frederic P. Shidler* | 1230 |
| Surgical Treatment of Coarctation of the Aorta. Further Experiences with the Use of the Subclavian Artery | *Harris B. Shumacker, Jr.* | 1235 |
| Aneurysm of the Hepatic Artery. Report of Three Cases | *John H. Steelquist* | 1241 |



Senile vaginal epithelium is low in glycogen, low in acid and (inset) low in protective Döderlein bacilli, encouraging growth of pathogenic organisms.



Normal vaginal epithelium is high in glycogen, is definitely acid and (inset) contains adequate Döderlein bacilli to combat pathogenic organisms.

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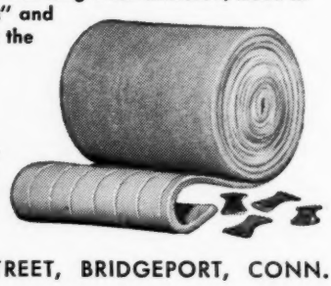

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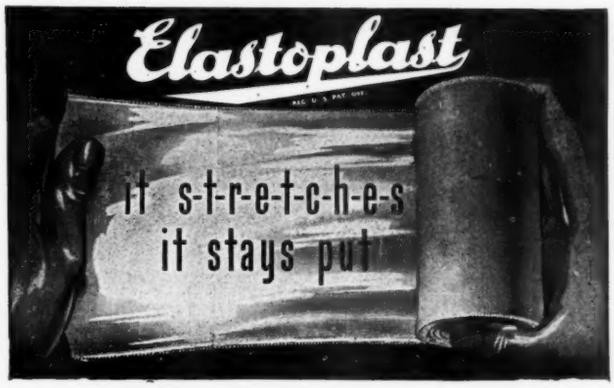


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# NOTES AND QUOTES

ONE of the world's most famous medical manuscripts—the 600 year old Codex Paneth—has been acquired by the Yale Medical Library. This rare, early medieval work containing 1,378 pages, all of them in excellent condition, is believed to have been the entire medical library of the University of Prague when it was founded in 1347 to 1348.

The beautifully colored illuminations, handdrawn by painstaking craftsmen, give an insight not only into the art of the early 14th Century but also to the amazingly advanced surgical instruments of the time. Many of the scalpels, surgical saws, forceps and orthopedic instruments shown in this manuscript look remarkably modern. In fact, some of the instruments shown in these manuscripts are still being used in slightly modified form, according to Frederick G. Kilgour, Librarian of the Yale School of Medicine, who announced the acquisition of the Codex Paneth.

*American wage earners have fewer accidents while on the job than they do out of working hours—at home, on the streets and highways, and in recreational pursuits. Nearly 70 per cent of the deaths from accidents and more than half of the non-fatal disabling accidents among workers occur during "off-the-job" hours. The predominance of non-occupational accident fatalities is borne out by the experience among males with industrial insurance in the Metropolitan Life Insurance Company. In this experience the proportion of accidental deaths occurring off the job varied with the occupation of the worker, according to the insurance company's statisticians. In a number of occupational groups all or nearly all of the fatal injuries were sustained off the job.*

AN artificial eye, operated by magnets causing the eye to move and even twinkle as effectively as the living eye it matches, has been developed at the Veterans Administration hospital in Boston, Massachusetts.

The "magnetic eye," as it has been called by its designers, already has been implanted into more than 150 New England veterans whose eyes have suffered injury or disease. The designers are Dr. Everett H. Tomb, Chief of the eye, ear, nose and throat section, and Dr. Donald F. Gearhart, Chief of the plastic eye and restorations clinic at the Boston V. A. Hospital. After six years of research Drs. Tomb and Gearhart have perfected a magnetized implant, the magnet of which is placed within clear, non-irritating plastic.

The artificial eye, being held close magnetically to the surgically buried implant, follows the implant's motion. The movement muscles of the removed eye, when attached to the implant, cause it to move in the same directions and at the same time, as the living eye. Likewise, the artificial eye's magnet, by following the magnet of the implant, causes the artificial eye to move in the same direction at the same time as the living eye.

Each plastic artificial eye is moulded individually to shape with modifying color pigments added to closely resemble the cosmetic appearance of the wearer's living eye. The color of the living eye is copied by brushing artists' oils on plastic discs. Colored rayon threads are embedded in the plastic to resemble veins.

*Examples of such groups are workers in cotton or woolen mills and in furniture factories, barbers, and operatives in shoe and clothing factories, among whom the non-occupational mishaps accounted for the entire accident death toll in the years 1951 through 1953. Other such groups are the white collar workers, among whom fewer than one in ten of the accident fatalities arose in the course of their employment. Even in occupations which involve appreciable accident hazards, off-the-job accident fatalities predominated in the insurance experience.*

*"The over-all results of this survey bring into sharp focus the need for intensifying the efforts against off-the-job accidents," the statisticians observe. "Much of the improvement in solving the accident problem in our country must come from reductions in home, highway, and recreational accidents."*

AN advance in suture packaging has been made by Davis & Geck, Inc., manufacturers of surgical sutures and specialties. Surgilope, a new, double-envelope, sterile, metal foil package is expected to eliminate glass suture tubes from the operating room. The outside envelope is



CONTINUED ON PAGE 40

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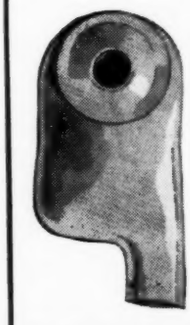

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# NOTES AND QUOTES

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*Among workers in our country, nearly 70 per cent of the deaths from accidents and more than half of the non-fatal disabling injuries occur off the job. The National Safety Council estimates that among the more than 60,000,000 employed men and women in the United States last year, there were approximately 44,000 accidental deaths; only 14,000 of them arose out of and in the course of employment. Of the 4,300,000 non-fatal disabling injuries sustained by workers last year, nearly 2,500,000 were non-occupational.*

DR. CASIMIR FUNK nearly lost a battle with his scientific colleagues when he coined the word "vitamin." Were it not for his persistence in pushing forward his bold hypothesis which laid the foundation for the entire subject of vitamins, the acceptance of these essential dietary substances might well have been long delayed.

These interesting facts in the life of Casimir Funk are included, among many others about the famed scientist, in a new book by Professor Benjamin Harrow, Head of the Department of Chemistry at City College of New York. The book, entitled "Casimir Funk: Pioneer in Vitamins and Hormones," has been published by Dodd, Mead & Co.

*Comforting news for the large number of Americans with gallbladder disorders is provided in a current report by statisticians of the Metropolitan Life Insurance Company. The company's experience among its industrial policy-holders shows a marked decline in the death rate from diseases of the gallbladder, including gallstones. Among women in the insured group the death rate from these diseases has declined more than three-fifths since the years shortly prior to World War II—from 7.7 per 100,000 for 1936 to 1938 to 2.9 per 100,000 for 1951 to 1953. Among males in the insured group the death rate was cut in half during the same period—from 3.4 to 1.7 per 100,000.*

*The statisticians also report that a long-term follow-up study of insured persons with a history of gallbladder disorders indicates that such persons have a relatively favorable mortality, although somewhat higher than the average for persons insured at standard premium rates.*

ETHICON, INC., leading manufacturer of surgical supplies, has just completed a package redesign program aimed at providing hospitals and medical personnel with greater facility in the identification and handling of surgical materials. Included in the redesign program, created by New York industrial designers Lippincott & Margulies, are suture containers devised for instant content identification, a crucial concern of operating room personnel.

In addition to the suture container which now provides easier handling, suture labels were redesigned to spotlight product type, size and code markings. The new label is gray, with a clean, legible logotype in red letters given secondary position on the label. A white area on the label is reserved to highlight product identification printed in black.

*The proof thus far presented that cigarette smoking is the cause of lung cancer is only made up of suspicion and coincidence, says Dr. William Rienhoff, Jr., in the May issue of Pageant Magazine. In his article "Go Ahead and Smoke," Dr. Rienhoff, a surgeon at Johns Hopkins and a long-time cancer researcher, objects to the many unscientific reports being pushed before the public, making millions of smokers needlessly fear they are doomed to die of lung cancer.*

*Dr. Rienhoff's main objections to the past year's "big scare" are two-fold. First, seeing his friends, patients and fellow doctors who smoke and enjoy it become frightened after reading all the reports, he says, it is wrong "on the basis of incorrect scientific assumption" to take this obvious pleasure away from them. Second, he believes that it is "dangerous science to jump to an unsubstantiated conclusion that cigarettes are the cause of lung cancer and then concentrate our lung cancer research on this avenue alone."*



CONTINUED ON PAGE 42

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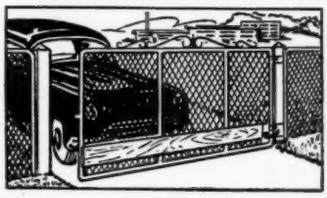

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# NOTES AND QUOTES

PARKE, DAVIS & COMPANY, which produced a major portion of the polio vaccine for the National Foundation for Infantile Paralysis at cost in 1954 and 1955, plans to make the vaccine commercially at a rate reaching 300,000 complete immunizations a week before the year closes.

Harry J. Loynd, President, said the firm—after being licensed by the National Institutes of Health—began to make the vaccine for distribution "through regular channels on the most equitable basis possible." List price, not including the doctor's fee, will be $6.00 for one complete immunization (three 1 cc. shots).

He emphasized, "Temporarily, at least, there will not be enough vaccine for everyone who wants it. The commercial vaccine will be available through physicians. Parents who want their children or other members of the family to have the vaccine should consult their doctor."

*The University of Buffalo is planning to establish the first school in the country for training limb fitters and brace fitters, it was revealed recently by Joseph E. Traub, Chief of the Prosthetic and Orthopedic Department of the University's School of Medicine, in an address to the Industrial Medical Association during the Industrial Health Conference.*

*"Until this time, all limb and brace fitters have been trained by the apprenticeship method, with no two apprentices undergoing the same training," Mr. Traub explained. "Therefore, there has always been a great difference in the quality of fitters. The proposed school will have a four-year curriculum and offer a Bachelor of Science degree. The establishment of this school is a very difficult task and it needs all the support it can get."*

*"There may be no experience more shocking to the human being than the loss of a limb," Mr. Traub continued. "There is a finality about it that in its first terrible impact is difficult to comprehend or believe. Therefore, it takes all the skill man is able to muster to provide a comfortable and functional replacement for this lost limb."*

A RADIATION control laboratory to study new radiologic problems posed by industrial use of radioactive material is now being constructed by Liberty Mutual Insurance Co., the nation's largest mutual casualty insurance company.

First of its kind to be built by an insurance company, the new laboratory is being established at the Boston firm's research center at Hopkinton, Mass. Chemical laboratories and other facilities for the study of industrial hazards will also be housed in the new structure, expected to be completed by November. These facts were disclosed recently in an announcement by S. Bruce Black, Liberty Mutual President.

"Construction of the new laboratory reflects the wide extent to which nuclear materials are now being used by industry and the resultant concern of insurance companies," Black noted. "This development has created a whole new category of problems for casualty companies," he said. "In 1954, some 2,400 organizations were using radio-isotopes as compared with only 86 such users nine years ago. Production of these materials and the equipment to handle them is already a $60,000,000 annual business. In the field of electric power it is estimated that 50% of new plants will be of the atomic type within twenty years."

*A joint attack upon a single type of cancer—the malignant melanoma—has been organized through a cooperative group research program between The University of Texas M. D. Anderson Hospital and Tumor Institute in the Texas Medical Center, Houston, and the University of Oregon Medical School, Portland.*

*The cooperative effort, organized in December, 1954, will be known as the "Melanoma Study Section," and is the second such group research effort organized by The University of Texas M. D. Anderson Hospital. The first was the "Cancer Eye Study Section," with the Iowa State College, the Oklahoma Agricultural and Experimental Station, and the Department of Genetics, The University of Texas, for the study of squamous ocular carcinoma in cattle.*

*The Melanoma Study Section plan combines the basic sciences and medical specialities available in a cancer research, education and treatment center, and in other institutions having scientific personnel and research facilities oriented in the research problems undertaken.*

*On February 15th the National Cancer Institute recommended approval of grants for the Study Section concerned with the diagnosis, chemotherapy and microbiologic studies of melanoma.*

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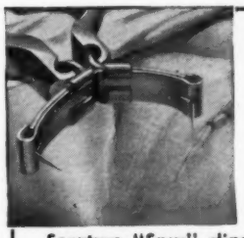

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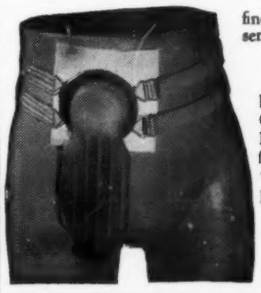

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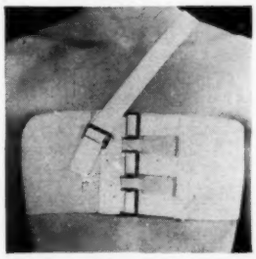

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## ADVERTISERS INDEX

Abbott Laboratories....21, 30
Aeroplast Corp.... 19
American Bakers Association.... 26
American Hospital Supply Corp.... 4
American Meat Institute.... 23
Ames Company, Inc.... 1
Astra Pharmaceutical Products, Inc... 29
Austenal Laboratories, Inc.... 9
Auto-Bumper Gate Co.... 41
Bard-Parker Co., Inc.... 34
Baxter Laboratories, Inc.... 4
Bristol Laboratories, Inc....
*Insert Facing Page* 36
S. H. Camp & Co.... 43
Chatham Pharmaceutical Inc.... 14
Ciba Pharmaceutical Products, Inc....
10, 15, 27, *Back Cover*
Cochrane Physicians' Supplies, Inc.... 39
Connecticut Bandage Mills, Inc.... 34
Cook County Grad. School of Medicine 36
Cutter Laboratories.... 6
Davis & Geck, Inc....12–13
J. A. Deknatel & Son Co.... 22
DePuy Manufacturing Co.... 39
Desitin Chemical Company.... 28
Dome Chemicals, Inc.... 37
Duke Laboratories, Inc.... 37
Ethicon Suture Laboratories, Inc....
*Insert Facing Page* 8
Freeman Mfg. Co.... 39
Gudebrod Bros. Silk Co., Inc.... 24
Hoffmann-LaRoche, Inc....
*Insert Facing Page* 24
Kling Photo Corp.... 41
Lederle Laboratories.... 25
Eli Lilly & Co.... 32
Little Manufacturing Co., Inc.... 43
The S. E. Massengill Co....
*Insert Facing Page* 16
Medical Aids, Inc.... 41
V. Mueller & Co.... 11
N.Y. Polyclinic Medical School & Hospital.... 36
Notes and Quotes....38, 40, 42
Orthopedic Frame Co.... 41
Murle Perry.... 43
Pfizer Laboratories, Div. of Chas. Pfizer & Co., Inc....8, 16, 44
Propper Mfg. Co.... 43
The Radium Emanation Corp....39, 41
Rajowalt Co.... 43
Richards Mfg. Co., Inc.... 43
H. W. Rutzen & Son.... 39
Seal-Ins Laboratories, Inc.... 39
G. D. Searle & Co.... 33
E. R. Squibb & Sons, Div. of Mathieson Chemical Co.... 18
The Surgeon's Mart....39, 41, 43
The Tower Co., Inc.... 39
The Upjohn Company.... 20
Wallace & Tiernan Products, Inc.... 41
Winthrop-Stearns, Inc.... 2
Zimmer Manufacturing Co.... 43

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